Journal of Neurosurgery

UNIVERSITY
JUL 29 1944
LIBRARY

JANUARY 1944

VOLUME I JANUARY 1944 NUMBER 1

JOURNAL OF NEUROSURGERY

[*J. Neurosurg.*]

MANAGING EDITOR

LOUISE EISENHARDT, 310 Cedar Street, New Haven, Conn.

EDITORIAL BOARD

GILBERT HORRAX, Boston, *Chairman*

A. ASENJO, Santiago de Chile
KENNETH G. MCKENZIE, Toronto
CAPT. W. MCK. CRAIG (MC), U.S.N.R.
LT. COL. R. GLEN SPURLING, M.C., A.U.S.

ADVISORY BOARD

ALFRED W. ADSON, Rochester, Minn.
HOWARD C. NAFFZIGER, San Francisco
BRIG. HUGH CAIRNS, Oxford, Eng.
HERBERT OLIVECRONA, Stockholm
CLAUDE C. COLEMAN, Richmond
WILDER PENFIELD, Montreal
GEOFFREY JEFFERSON, Manchester, Eng.
ERNEST SACHS, St. Louis, Mo.

PUBLISHED BI-MONTHLY

FOR THE HARVEY CUSHING SOCIETY BY

CHARLES C THOMAS

220 EAST MONROE STREET, SPRINGFIELD, ILLINOIS, U.S.A.

Copyright, 1944, by Charles C Thomas. Subscription rates: $7.50 a year in the United States, Canada and Latin America; $8.00 a year in other countries; single copies, $1.50 postpaid. Application for entry as second-class matter is pending.

JOURNAL OF NEUROSURGERY

EDITORIAL NOTE

WITHIN the past thirty years neurosurgery has become a firmly established branch of medicine, and the need for a channel of publication has been felt for more than a decade. The only journal devoted to the subject which has existed to date has been the *Zentralblatt für Neurochirurgie* established in 1936 at Berlin by Dr. W. Tönnis and the late Professor Otfrid Foerster. The journal was still in existence in 1939, but no issues later than that date have come to our notice.

Since neurosurgery as a specialty owes its origins largely to British and American surgeons, it seems the more fitting that a special journal in English should now be established. Since the outbreak of war in 1939, there has been less interchange between British and American neurosurgeons than before, and in each country there has also been less exchange of thought between individual neurosurgeons. Similarly, contacts between North and South America have tended to be restricted as a result of wartime limitations, and in establishing the present journal The Harvey Cushing Society, taking its name from the foremost neurosurgeon of our time, has wished to embrace the interests not only of English-speaking neurosurgeons in the larger sense, but of Pan-American neurosurgeons as well. When international communications are reestablished, it is hoped that the Journal will have worldwide representation. We feel especially fortunate, therefore, that the Journal can include in its Editorial and Advisory Boards Dr. A. Asenjo, Director of the Pabellon Cushing in Santiago, Chile, and our distinguished Swedish colleague, Dr. Herbert Olivecrona, whose school of neurosurgery developed in Stockholm has been worldwide in its influence. The Society hopes at a later date to have representation from other parts of the world in which neurosurgery flourishes.

The Society is glad in the first number of the Journal to be able to include the paper of our member, Franc Ingraham, and his colleague, Orville Bailey, since it records a technical advance which may prove comparable in importance with the introduction of the silver clip, endothermy and suction. The Society will welcome papers of this character as well as records of other types of neurosurgical and neurophysiological experience based on human material (see statement on third cover). The Editors expect also in the future to publish book reviews and possibly reviews of general literature. The editorial office will be glad to receive books for review.

That the first number should be limited to contributions from the United States is a purely fortuitous circumstance stemming from the fact that papers already promised from England and from South America have not yet reached the editorial office. Later numbers of the Journal will have material from these sources, and the Editorial Board takes this opportunity of extending a hearty invitation to our other colleagues overseas to submit contributions that may be appropriate. With the war in its most active phase, we would direct attention to the need for prompt record of wartime experiences. The recent reports of Major Peter Ascroft, and of Hugh Cairns and his colleague, H. Holbourn, have set a high standard for clarity and force of presentation, and we hope that the Journal may be fortunate enough to secure wartime contributions of this quality. We cannot close without expressing deep sympathy to our British colleagues in the untimely death while on active service of Major Kenneth Eden, whose posthumous paper entitled, "Mobile neurosurgery in warfare. Experiences in the Eighth Army's campaign in Cyrenaica, Tripolitania and Tunisia," has just been published in the *Lancet* (Dec. 4, 1943).

THE EDITORIAL BOARD

Dr. Cushing operating in the Peter Bent Brigham Hospital before The Harvey Cushing Society at its first meeting, May 6, 1932. (*Courtesy of Dr. R. U. Light.*)

SOME OF HARVEY CUSHING'S CONTRIBUTIONS TO NEUROLOGICAL SURGERY

GILBERT HORRAX, M.D.

Department of Neurosurgery, The Lahey Clinic, Boston, Massachusetts

(Received for publication December 16, 1943)

TO THE OLDER GROUP of neurological surgeons in this country and abroad and to many members of the Society which is sponsoring the *Journal of Neurosurgery*, the name of Harvey Cushing has stood for a large proportion of the advances which have been made in this specialty since the time, some fifty years ago, when Sir Victor Horsley may be said to have established it as a separate branch of surgery. Indeed, a large number of those practicing neurosurgery today had the privilege of seeing Dr. Cushing at work, of hearing many of his addresses to medical societies, or of benefiting immediately by the contributions which he was making continuously to his chosen field. To those who followed his career and to others who have been concerned with the advances in neurological surgery, a recital of his outstanding accomplishments would be as out of place as it would be unnecessary, since they are well known alike to his pupils and to his many admirers. However, during the last decade a large, younger generation of neurosurgeons has arisen, and it is perhaps particularly to them that this communication may be of interest.

It would be impossible in the space of a short review such as this to do more than touch upon what have seemed to be Dr. Cushing's major communications as they have influenced neurosurgery directly. Many of his brilliant experimental and laboratory studies have been omitted or merely mentioned since I have undertaken to confine myself for the most part to his purely technical contributions. At times, however, the laboratory and the clinic overlap so intimately that the story of one would be quite incomplete without the other.

In order to get a background for the life and work of Harvey Cushing, we must for a moment look at the status of this newly launched specialty up to the time when he appeared upon the scene. Not until the era of anesthesia and antisepsis, and particularly not until the beginnings of cerebral localization (*circa* 1870) had operations upon the brain and spinal cord advanced appreciably since medieval or ancient times. Soon after this, in the middle eighties of the nineteenth century, a very few, and very occasionally successful, operations upon brain tumors, brain abscesses and spinal cord tumors were performed. Finally, during the decade from 1890 to 1900, Victor Horsley by his vigorous pioneering and tireless physiological and pathological investigations, succeeded in getting before the medical profession the fact that much more could be accomplished surgically for certain lesions of the central nervous system than had previously been supposed. However, the technic of brain operations at this time was crude, and was influenced largely by

general surgical methods which we now know cannot be applied to such delicate performances. Even as late as 1906, Horsley[32] himself made the following statement, "In fact, the advance in technique of the surgical treatment of diseases of the brain and the spinal cord has been relatively less than the improvement in our knowledge of the seat and nature of the diseases for which surgical intervention is useful and necessary." If this was true of Horsley's own work, it was even more so of the leading surgeons in Europe, notably Bergmann, Kocher, Krause, von Eiselsberg, Chipault, Broca and others, all of whom had made signal contributions and had written extensively on the subject of cranial and spinal operations even though their results were certainly not nearly so good as those of Horsley.

In other words, at the turn of the twentieth century it was evident that a large new field of surgery was opening, indeed had been opened, but that in this new field no one had as yet appeared who fully appreciated and was able to develop a surgical technic which was sufficiently delicate and meticulous to make operations, particularly on the brain, produce results at all comparable to the results of operations elsewhere in the body. It was at this juncture that Harvey Cushing in Baltimore began to devote himself almost entirely to the study and practice of neurological surgery at The Johns Hopkins Hospital and in the Hunterian Laboratory of the medical school.

The results of this study and practice began almost immediately to appear. In 1900, Cushing[2] published the details of a method for the total extirpation of the gasserian ganglion. In essence, it was a refinement of the so-called Hartley-Krause procedure, but because of this refinement a complete removal of the ganglion could be accomplished for the first time with certainty, whereas by the older methods, removal almost always had been either incomplete or uncertain. The operation described in this article is, to all intents and purposes, the same subtemporal approach which is used today for division of the sensory root behind the ganglion. Cushing's illustrations show that not only the ganglion but also the sensory root of the trigeminal nerve was extirpated, but it was not realized until the work of Spiller and Frazier[34] a year later that it was necessary only to divide the root, thus making removal of the ganglion superfluous.

During the next five years there were several notable contributions. In 1901, Cushing's[3] announcement of a regulating mechanism in the vasomotor center for the control of blood pressure during cerebral compression was an epoch making event. This study was and is so important for the understanding of clinical states, operative complications, traumatic brain conditions and the like that it must be included here, although this review is primarily from the clinical standpoint. As Cushing himself stated,

> The fact that cerebral compression occasions a rise in blood pressure is universally known, but it does not seem to have been recognized that the degree of this elevation occurs *pari passu* with the degree of compression (measured in millimetres of mercury) to which the medullary centres are subjected.

The article contains beautiful kymographic records showing synchronized

blood pressure and intracranial pressure tracings. The author summarized his findings as follows,

> As a result of these experiments a simple and definite law may be established, namely, *that an increase in intracranial tension occasions a rise of blood pressure which tends to find a level slightly above that of the pressure exerted against the medulla.*

In 1903, Cushing's[4] first formal paper on the routine taking of blood pressure during operations and in the clinic was read at the Boston Medical Library. He had introduced the Riva-Rocci blood pressure instrument into this country in 1901 and had made reference to its use in his Mütter Lecture in Philadelphia the same year. The importance of this measure as a routine in surgical anesthesia charts needs no emphasis since it has become a standard procedure in every first-class hospital. In this, as in other important innovations, Cushing had to reiterate his plea many times before routine blood pressure determinations during operations were adopted. In 1905 at Cleveland,[6] he gave the following pertinent reasons for blood pressure readings, "Such a record not only furnishes instructive . . . general data, but often furnishes a means of properly interpreting the effects, beneficial or otherwise, of the various operative steps."

A minor contribution in 1904 was the description of a pneumatic tourniquet for the control of scalp bleeding during operations.[5] This was an improvement on tourniquets previously used, but he himself later discarded it for a simpler device which was used until tourniquets were entirely discarded, probably because of the advent of novocain and adrenalin anesthesia at the time of World War I.

In the following year (1905) two highly significant papers appeared. The first of these was concerned with the operative treatment of intracranial hemorrhage in the newborn.[7] Until that time this unfortunate condition had been considered hopeless and the pitiable victims who survived the hemorrhage were destined to various states of spastic paraplegia, usually with seriously impaired mentality, blindness and other evidences of cerebral damage. Cushing was able to report four operative cases with two recoveries from serious subdural hemorrhage in infants from three to eight days old. Subsequently (1910)[15] he reported 12 further cases with recoveries in about half the patients and without the development of spastic paraplegia. In this second article he likewise stated that one of the infants upon whom he had operated in 1905, "is now a healthy and normal child of five years of age."

Cushing's other important paper in 1905 related to palliative decompression for inaccessible brain tumors.[8] It had long been known, through the work of Horsley, Sänger and others, that an opening in the skull accompanied by incision of the dura in patients harboring a brain tumor would almost always relieve headaches and other pressure symptoms and preserve eyesight by allowing choked discs to subside. Heretofore, however, these operations had been performed, as a rule, either at the supposed site of the tumor, whether or not the tumor had been found, or, as advocated by Sänger[33] (1902), in the right postcentral region in right-handed persons. In

other words, the procedure had been used by others apparently as an adjunct to either possible or probable tumor removal, or had been done in an area which was covered only by scalp, and in the latter instances often caused unsightly protrusions or even made incipient paralyses worse because of hemorrhage or edema in the protruding herniation. Cushing's invaluable contribution was, first, the fact that he advocated decompression often as a purely palliative measure when there was no expectation of the ability to remove an inaccessible tumor, and secondly, his advocacy of the use of an area that was protected not only by scalp but also by muscle, that is, the low right

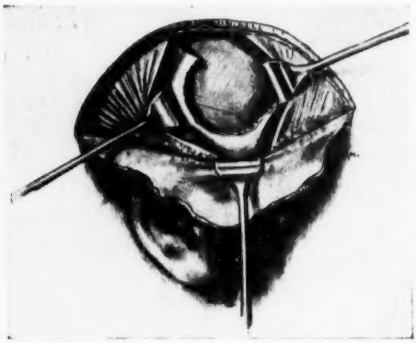


FIG. 1 (*above*). Sketch of "intermusculo-temporal" decompression as first employed. Later, a straight, vertical incision was used.[8]

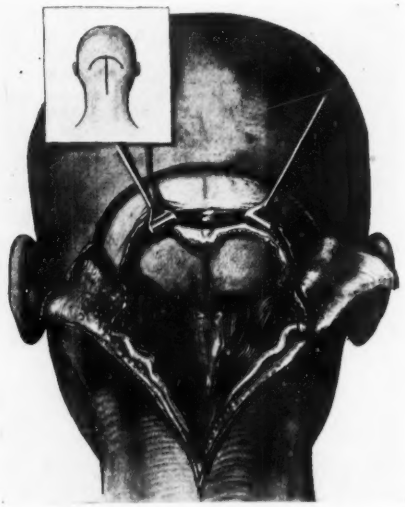


FIG. 2 (*right*). The "crossbow" incision for suboccipital decompression and exploration.[8]

temporal region in right-handed persons for supratentorial growths and the suboccipital region for tumors below the tentorium. Referring to his 1905 paper, he himself has expressed the situation regarding "decompression" at the time when this subject was so much in vogue, and summed it up in his address at Cleveland in 1910[15] in these words,

> That relief of pressure in many instances had unexpectedly followed unsuccessful explorations for tumors had long been a matter of general knowledge, and Horsley, Weir and other forerunners in the work had been led to propose simple trepanation as an intentional palliative measure; but I am unaware that any author had previously suggested a purposeful decompression irrespective of possible tumor removal, and the utilization not only of a "silent" area but also of overlying muscle to prevent too great protrusion of the herniating brain, or had ever emphasized the importance of decompressing at a distance from the growth as a preliminary measure should the brain prove to be under great tension.*

* So far as I have been able to discover, this contention of Cushing is correct. Horsley (*Brit. med. J.*, 1893, 2: 1365–1367), referring particularly to headache, vomiting and choked discs, made the following statement, "I wish now to advocate, as I have done before, that the opening of the skull should be undertaken for the purpose of relieving these symptoms especially. . . . I operated as much with the direct object of relieving intracranial tension as of exploration with the view of attempting the removal of the

The value of this type of palliative decompression in those early days hardly can be overemphasized. It relieved an infinite amount of suffering, preserved vision, and allowed many patients to get back to active and useful work, sometimes for years. Indeed, in not a few persons the tumors later became localizable and were removed successfully, whereas if they had not been decompressed death or blindness in all probability would have resulted. In the 1905 article concerned with decompression an illustration of the "intermusculo-temporal" operation is given, together with an illustration of the "crossbow "incision for suboccipital craniotomy. The latter operation, as well

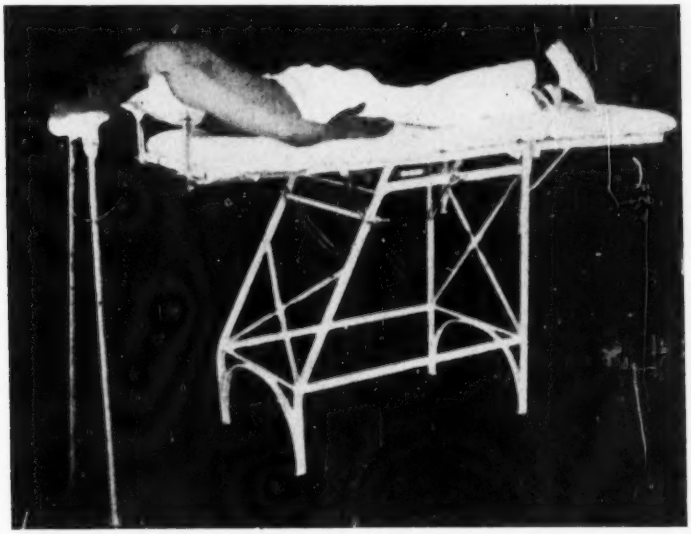


FIG. 3. Shoulder supports and crutch for holding head employed to safeguard respiration in operations requiring prone position.[9]

as the subtemporal procedure in simplified form, became the standard for many years (Figs. 1 and 2).

Reference was made earlier to the importance of the refined and meticulous technic which Harvey Cushing inaugurated in neurosurgery. The many and intimate features of this technic constitute one of his major contributions to the subject, in fact, it was largely because of his extreme attention

growth." In 1906, after the appearance of Cushing's article, Horsley[32] wrote the following, "To sum up then, during the past twenty years we have learnt that . . . we can with certainty avert blindness by opening the subdural space early in cases of intracranial disease. [Preferably in the basal temporal region of the right side, that is, assuming that no attempt is made to attack the disease itself.]" From the first of these quotations, it is clear that Horsley was, of course, familiar with and practiced the principle of decompression, apparently at the site where he was exploring for a tumor. In the second quotation he does refer to subtemporal decompression as a palliative measure, but this was after Cushing's paper had appeared, and furthermore, the invaluable principle of utilizing careful closure of the temporal muscle over the decompression is not mentioned.

to details that he was able to accomplish so much for patients with disorders of the nervous system. In an address before the St. Louis Surgical Society in 1908,[9] Cushing set forth at considerable length the methods which he had found useful in performing various cranial operations. Essentially similar reiterations are to be found in his monographic contribution to Keen's *System of Surgery*[10] (1908) and in a paper[11] (1909) delivered at the meeting of the American Medical Association in June, 1908. The description starts with the general preparation of the patient, the careful shaving of the head just

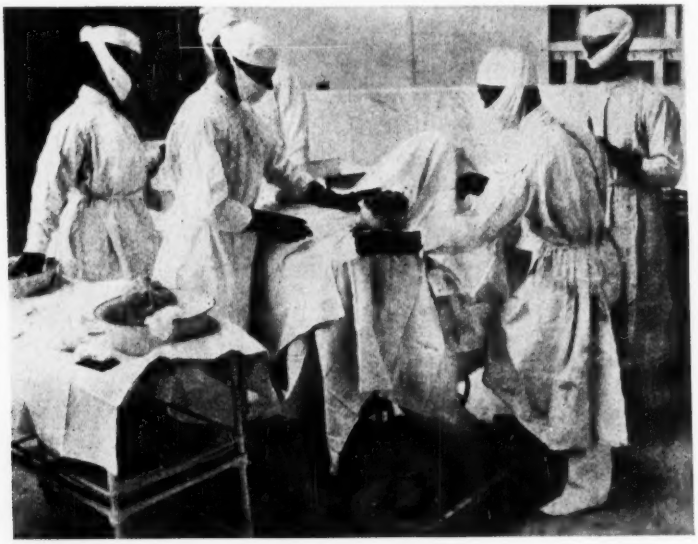


FIG. 4. Dr. Cushing and his operating team at the Johns Hopkins Hospital. Note bloodless operative field and hood covering anesthetist.[9]

before operation (not the previous night as heretofore practiced), the position on the table (Fig. 3), the anesthesia given by a trained anesthetist who kept a pulse, respiration and blood pressure chart, the preparation of the operative field with bichloride solution and alcohol, and the device of scratching out on the scalp the proposed line of incision. There follow minute directions as to the control of hemorrhage in the various tissues encountered, the performance of osteoplastic craniotomy and other operations, as well as the steps of certain intracranial procedures (Fig. 4). The reduction of increased intracranial pressure by means of lumbar puncture during the course of an operation was advocated—a new feature and extremely important at this stage of neurosurgery in order to prevent cortical rupture while opening the dura. Not the least of the principles advocated was the *closure of the wound* to which especial care was directed, *including closure of the galea** and meticu-

* One of Dr. Cushing's favorite themes in later years when questioned concerning his surgical contributions was, "Tell them that I closed the galea."

lous approximation of the skin edges (Fig. 5). In his 1908 articles, Cushing refers to his method of combining an osteoplastic exploration with a subtemporal decompression when this is necessary. A later paper (1909)[12] was devoted to an extended description of this procedure which became a recognized standard (Fig. 6).

Perhaps the highest tribute which can be paid to Cushing's attention to detail is contained in a statement he himself made in 1908[9] concerning the healing of wounds. He says, "In something over 350 craniotomies I have never seen an infection, even a superficial stitch abscess, and have ceased to regard

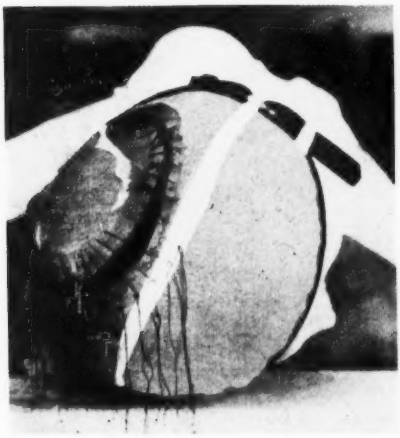


FIG. 5 (*left*). Meticulous approximation of scalp by interrupted fine silk sutures. Note tourniquet in place and scalp covered with gauze.[9]

FIG. 6 (*right*). Illustration of "combined exploration and decompression."[12]

the chance of sepsis as a possible complication of these operations." Can any neurosurgeon of the present day say as much?

Although chronologically somewhat out of place, it is pertinent to mention at this juncture a device for the control of intracranial hemorrhage, with which the name of Cushing will always be connected. This is the silver clip outfit, a description and illustration of which appeared in 1911.[16] Modifications of the original clips have since been made, but essentially the ones used today by all neurosurgeons are the same as those first described (Fig. 7). They constitute one of the major advances in the control of bleeding from dural and cortical blood vessels, and have been only partially superseded by electrocoagulation.

This 1911 article on the control of bleeding is highly important for a further reason. In it the author describes the use of muscle, bits of living tissue or well solidified blood clots as a valuable aid in arresting surface oozing or bleeding on the dura. Apparently this was the earliest reference in the literature to such a method of hemostasis, although Cushing stated in a

footnote that Dr. Lund had reported having seen Horsley demonstrate the use of muscle in the same way the year previously. However, Cushing further remarked, "Since this device for checking bleeding was first hit upon some two years ago, we have made frequent use of it, with most satisfactory results."

From 1906, when Cushing read his first paper dealing with conditions affecting the pituitary gland, he continued to make numerous and important contributions to our knowledge of the physiology and pathology of this structure, and these in turn led to great advances in the surgical attack upon tumors of the hypophysis both by him and by neurosurgeons throughout the world. It is not within the scope of this review to dwell upon his experimental contributions, in which his numerous distinguished co-workers often collaborated, and to whom he has given abundant credit. It must suffice to say that his earlier laboratory work coupled with his rapidly accumulating clinical material was put together in his first book, *The Pituitary Body and Its Disorders*, in 1912.[17] While much had been written by others concerning the hypophysis before this time, and while a number of other surgeons had reported operations upon tumors of the gland, Cushing not only reviewed all the existing literature but also was able to report the most extensive and most successful series of operations upon the pituitary gland that had been undertaken up to that time by any one person. Undoubtedly, his results were to be attributed to two factors, first, his wide experimental laboratory experience with the gland in animals, and secondly, his consummate skill as a surgeon. The operation which he used for the most part in his earlier pituitary work, and indeed until about the year 1927, was a transsphenoidal approach which he modified and improved from the procedures used by A. E. Halstead and Hirsch. By Cushing's method a considerably larger exposure of the base of the sella could be obtained, and consequently probably a better decompression or evacuation of the sellar contents (Fig. 8).

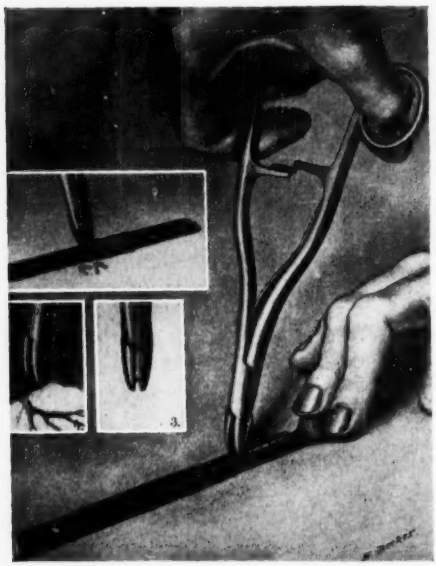


FIG. 7. Cushing's silver clip outfit, showing method of application to a blood vessel.[16]

A final report on Cushing's pituitary patients, whom he had operated upon at the Peter Bent Brigham Hospital, Boston, between 1913 and 1932, was made by one of his pupils, W. R. Henderson,[31] in 1939. There were 338

verified tumors in the series, and all but 3 of the 319 survivors were heard from after their discharge from the hospital. Since the last patient operated upon was in 1932, the follow-up period was from five to twenty-four years, as Henderson's data were obtained in 1936 to 1937. This report shows in convincing fashion Cushing's unexcelled supremacy in the surgical treatment of pituitary disorders. His total operative mortality for the chromophobe adenomas (260 patients) was 4.9 per cent, reduced to 2.4 per cent during his last ten years. For acromegalics (67 patients) the operative mortality was somewhat higher, namely, 8.6 per cent. None of the 11 patients with

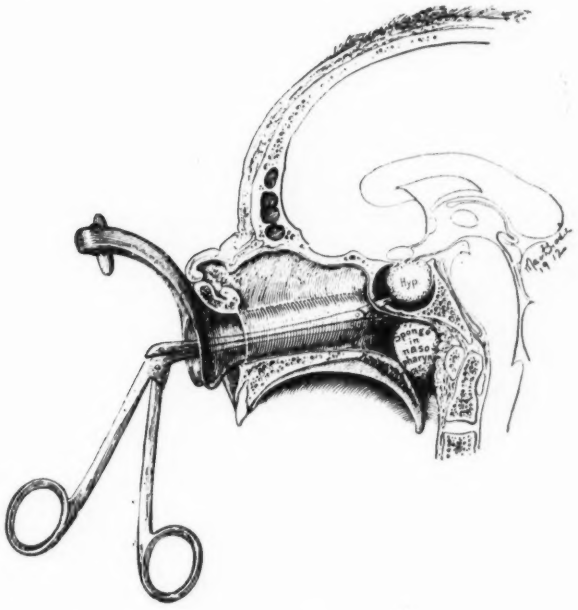


FIG. 8. Transsphenoidal approach to hypophysis (diagrammatic) showing beginning exposure of base of sella turcica (Cushing, H.: *J. Amer. med. Ass.*, 1914, *63*: 1515–1525).

adenocarcinoma of the gland died after operation. The increasingly good results of transsphenoidal and of transfrontal operations, and of both when followed by roentgen-ray therapy was shown. By a combination of the more complete removal of growth by an intracranial, transfrontal procedure, followed by radiation, 87.1 per cent of Cushing's patients so treated had remained free of recurrence at the end of five years.

From the beginning of his specialization in the field of neurosurgery, Harvey Cushing was particularly interested in the problem of brain tumors, necessarily no doubt because an ever increasing number of patients so afflicted came to him for help, but also almost certainly because these serious lesions intrigued him and demanded his utmost in skill and ingenuity. It was in dealing with the problems, diagnostic and surgical, concerning brain tumors that he contributed so greatly to our knowledge of these growths in

their manifold relationships. Due to his superlative operative technic, together with his infinite patience, he was able very early in his career to surpass the efforts of all those who had preceded him in dealing successfully with intracranial neoplasms. As far back as 1909,[13] he reported what were then brilliant results in a series of thirty-five suboccipital operations for presumed cerebellar tumors. Operations on the cerebellum in those days were thought to be the most dangerous of all intracranial procedures, and many authorities felt that cerebellar tumors were practically inoperable. Cushing, however, reported 13 successful tumor extirpations, 17 palliative suboccipital decompressions, and 2 inoperable tumors exposed. There were only 3 deaths in the series. In this and subsequent articles, he urged his belief that, contrary to the accepted ideas, cerebellar growths were even more favorable for operation than those above the tentorium. On two occasions in 1910, Cushing reported on operative experiences with brain tumors in general. In his William Mitchell Banks Memorial Lecture in Liverpool,[14] he stated that during the past ten months he had operated upon 64 brain tumor patients. There were 8 fatalities, a mortality of 12.5 per cent. "16 cases after removal and 21 cases after decompression are, to be conservative, greatly benefited and a number of them probably cured, making a percentage of 57.8 out of the 64 patients that have regained, temporarily at least, a full measure of health." He contrasted these figures with those given by Oppenheim in a recent communication which recorded the results of 27 tumor operations by competent surgeons during the course of three years. Of these, 2 patients were regarded as cured, 6 much improved and 1 improved; but about half of the 27 died of shock, hemorrhage or other operative complications. Again in 1910,[15] Cushing reported upon his last 100 patients with brain tumor, saying, that in 30 instances there had been tumor extirpations or cyst evacuations with apparent cures, and 67 palliative procedures. There were only 11 deaths and none of the "oldtime postoperative complications."

These figures may not sound very optimistic now, but it must be recalled that the most eminent neurologists of those days (Starr, Knapp and Mills in this country, and others abroad) had estimated from collected operative and postmortem material that only between 5 and 10 per cent of all brain tumors were operable, and in a large series collected from the literature Knapp found the immediate operative mortality to be 32 per cent. Furthermore, Knapp stated that a study of the cases reported as "recovered" showed that for the most part the patients merely lingered on "paralytic, epileptic or blind." Cushing's early accomplishments must therefore be viewed in the light of these facts and it will then be realized what strides he had already made. A further and extremely enlightening comparison of his results with those of the outstanding surgeons of other countries occurred in his discussion, published in 1915, of Professor Küttner's paper on brain tumors at the meeting of the American Medical Association in 1914.[18] Küttner gave his own operative mortality as 45 per cent and estimated the mortality in Berlin (Krause) at 50 per cent, and in Vienna (von Eiselsberg) at 38 per cent. A

study of Tooth's statistics from London (largely Horsley) approximated 32 to 37 per cent of immediate operative deaths. Cushing presented statistics based on the 130 patients he had operated upon in Boston only, since the data on his older Baltimore series were not then available. This was, however, a series comparable in point of number to those of the German and Austrian clinics, but considerably less than the number from Queen Square. Cushing's total case mortality was 8.4 per cent, a figure which was epoch making and almost unbelievable for that era. The key to his success is summed up in the final paragraph of his paper, thus,

> Specialization with some knowledge of neurology, skilled assistance—for intracranial operations are not star performances—familiarity with the safe and respectful handling of the central nervous tissues, which is best acquired by the experiences of the experimental laboratory, and painstaking, scrupulous technique, are the chief elements of success. An observance of these things will not make more tumors accessible, but it will permit the removal of those that are accessible to be more often accomplished and render those that are not, capable in a larger percentage of cases of being safely palliated.

In this discussion of Küttner's paper, Cushing had taken up in some detail the high operative mortality which prevailed not only for brain tumors in general, but in particular for the benign, encapsulated acoustic, or cerebellopontile angle growths. These tumors were made the subject of a monograph in 1917,[19] and this book was destined to become, as had *The Pituitary Body and Its Disorders*, a veritable landmark in brain surgery. Previous attempts at partial or complete removal of these deep seated, yet apparently favorable growths had been highly disastrous, and the prevailing mortality even with an occasional success was at least between 70 and 80 per cent. In his book, Cushing gave the details of what he termed an intracapsular enucleation of acoustic tumors, accomplished after a bilateral suboccipital exposure by means of the "crossbow incision" (Fig. 9). By this method, as much as possible of the contents of the capsule was evacuated by painstaking curettage and careful hemostasis, but the capsule itself, with its vascular connections to the pons and elsewhere, was not removed. This meant, of course, that most of the tumors would recur after greater or lesser intervals, unless they became quiescent, but even so, the operation was an immense step forward. In many instances, patients remained perfectly free of symptoms for five to ten years, in some cases longer, and likewise, some with recurrent tumors were operated upon again with success. Cushing's operative mortality for these growths at the time his book was published was in the neighborhood of 20 per cent in contrast to the *circa* 75 per cent mortality elsewhere. Within a relatively short time his mortality dropped to 10 per cent and even lower. In any case, Cushing's careful, very complete intracapsular operation for the first time offered patients with these tumors a reasonably safe procedure with a good chance of getting back to active normal life for a period of years, and thus revolutionized acoustic tumor surgery.

During the last part of his surgical career Dr. Cushing became more and more engrossed in the problems concerned with intracranial tumors, but

FIG. 9. Successive steps in the intracapsular enucleation of acoustic neuromas. The tumor exposed by retraction of cerebellum, its contents removed by blunt spoon, and finally, only the loose capsule left in place.[19]

before resuming a review of his efforts in this respect we must turn for a moment to two other contributions which were interspersed among those relating to tumors.

In 1917, he went overseas as director of Base Hospital No. 5 of the U. S. Army. The hospital took over a British Unit in northern France, but Dr. Cushing and various younger members from time to time were soon sent up to a British Casualty Clearing Station not far behind the front. It was here that he developed what was to become the standard treatment of penetrating gunshot or shell wounds of the brain. The general principles of this treatment hold good today. A summary of his method was published in the *British Medical Journal* early in 1918.[20] Cushing's chief contribution here was the careful and thorough débridement of the track of the missile in the brain by means of a catheter to which suction was applied by a hand syringe (Fig. 10). He stressed particularly the removal of all indriven bone fragments, emphasizing that these more than indriven metal were likely to be the source of future infection. He reported the results in a large series of these serious penetrating wounds in a comprehensive article in the *British Journal of Surgery* later in 1918,[21] and was able to show a remarkable reduction in the

mortality from the previously accepted rate. Thus, in 133 patients with wounds penetrating the dura, his mortality for the first 44 operated upon was 54.5 per cent (the usual accepted mortality). For the second 44 cases his mortality was 40.9 per cent, and finally, with accumulating experience, his mortality for the last block of 45 cases was 28.8 per cent.

The radical operation of sensory root division or avulsion for trigeminal neuralgia had, during the first two decades of the twentieth century, become

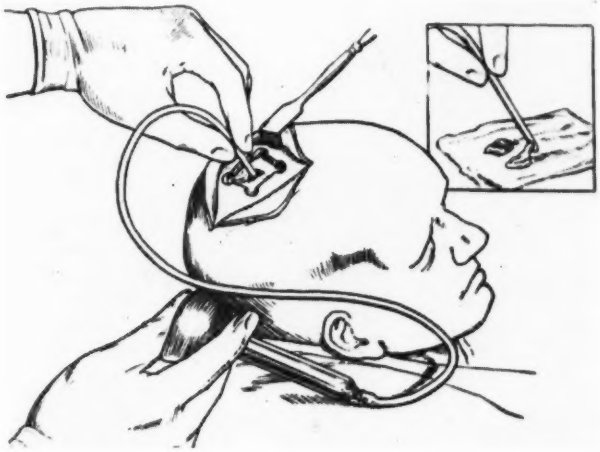


FIG. 10. Suction method for débridement in penetrating gunshot wounds of the brain.[20]

a fairly standardized procedure with an increasingly low mortality rate in the hands of skilled neurosurgeons. Among the best, however, this rate was somewhere between 1 and 2 per cent. In 1920,[22] Cushing published the statistics of his entire series of 322 ganglion or sensory root operations in which there had been but 2 deaths, a mortality of 0.6 per cent. These fatalities occurred in his ninth and thirty-fourth cases, leaving 298 consecutive operations without a fatality. So far as I am aware, this accomplishment surpasses that of any published record for this procedure.

We may return now to a consideration of Harvey Cushing's further outstanding contributions in the realm of brain tumor surgery. To make these contributions possible, detailed records of all his patients, including complete operative notes usually accompanied by his own sketches, pathological records of operative and postmortem material, photographs of the patients—all these and many other minutiae assembled by himself and his co-workers were brought to bear.

In the Cavendish Lecture for 1922,[23] he coined the term "meningioma" for the group of tumors heretofore listed by a variety of names, but usually

that of dural endothelioma. Using his extensive material he was able to pick out from the whole mass of these tumors different groups which always grew in specific locations, often giving specific symptoms, so that, before operation, they could be recognized and operative plans laid accordingly. This grouping of the meningiomas was an enormous step forward in our operative attack upon them, because, to a large extent, the extreme hazards of their removal could be foreseen in many instances and certain necessary precautions taken. Thus he added directly to the technic of the operating room, in a way which he himself described in the last paragraph of his lecture,

> What enables us, even in our present imperfect way, to detect, to localize, and finally, aided by all the paraphernalia of a modern operating room, to remove a brain tumour, is merely the application of most diverse fragments of knowledge contributed by countless workers in bygone ages, brought together from the ends of the earth and concentrated on a single act.

A somewhat similar, but more extensive study of the large glioma group of brain tumors was made in conjunction with Percival Bailey in 1926.[1] This marked the beginning of our pathological grouping of these tumors in which their pathology was correlated with their life histories and clinical characteristics, and, just as in the grouping of meningiomas, has been of enormous aid in knowing how to deal with these growths surgically. Other, more specific communications grew out of this original study, as evidenced in 1931[26] when he analyzed his experiences with the cerebellar astrocytomas. As he pointed out in this article,

> What has been chiefly contributory in recent years to the success of operations for intracranial tumors has been the tendency of those interested in the subject to concentrate upon the behaviour and traits of special tumors in special situations.

This special concentration brought out the knowledge which gradually was reached about 1925 or 1926, that to effect a permanent cure of a patient harboring an astrocytomatous cyst, it was essential to remove completely the solid portion of tumor within the cyst, whether this was a relatively small "mural nodule" or whether it might be solid growth as large or larger than the cyst itself (Fig. 11). Likewise, because of his concentrated study, he was able as early as 1922 to predict the presence of an unseen, deep, centrally placed cerebellar tumor and to remove it after transection of what looked like normal cerebellar vermis.

In 1927, Dr. Cushing was invited to give the Macewen Memorial Lecture in Glasgow, and he chose for his subject a discussion of the so-called olfactory groove meningiomas.[24] He called attention to the syndrome which Foster Kennedy had described in connection with the diagnosis of these and other growths in this locality, but stressed particularly the definite chronology of symptoms as of specific diagnostic importance for the meningiomas. But more important from the neurosurgical aspect was his discussion in this lecture of the first employment of electrosurgery in the removal of brain tumors. In introducing the subject, Cushing says,

When I first had the good fortune to see this loop being used bloodlessly to scoop out bits of tissue from a malignant tumour for purposes of biopsy, I foresaw that a new tool had been put into our hands to facilitate the piecemeal removal of . . . tumours. With Dr. Bovie's co-operation, during the past few months I have gained sufficient familiarity with the instrument to realize that it holds out untold possibilities for the future of neuro-surgery.

How true was this prophecy, the present generation of neurosurgeons can attest.

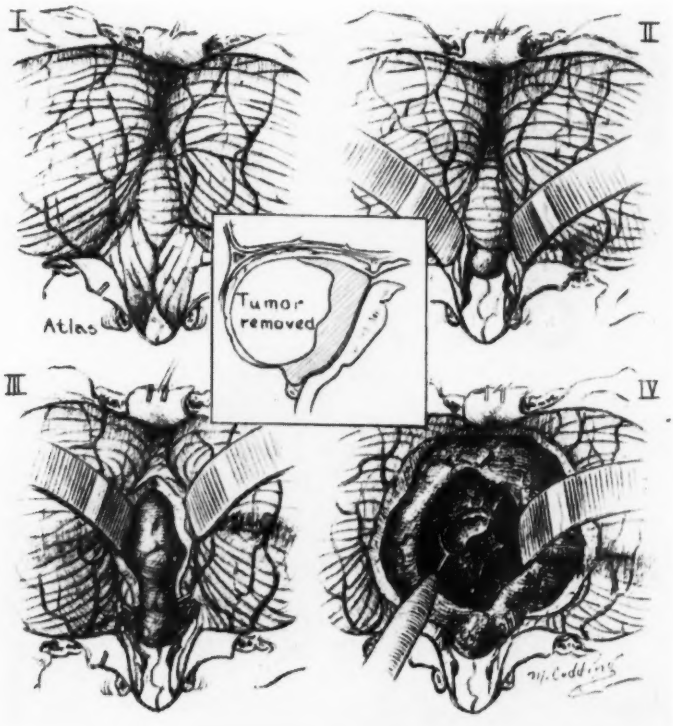


FIG. 11. Removal of large solid portion of astrocytomatous cyst of cerebellum by electrosurgery.[26]

Among other things the Macewen Lecture produces further evidence of Harvey Cushing's consummate patience and attention to technical details. After describing the use of the new electrosurgical apparatus in an operation for a large olfactory groove meningioma, he adds the following sentences which are sufficiently enlightening and significant to quote at length,

As matters stood, from the time when the scalp was novocainized to the final closure and dressing, seven hours were consumed . . . . To the surgeons who may be accustomed to speed

up their operations this may appear to have been an unnecessarily prolonged and formidable procedure. All said and done, it is the final result that counts, and having been brought up to believe that convalescence is shortened by attention to the technical details while the patient is on the operating-table, I have no dread of a long session . . . .

Enough has been said to indicate that we now have at our command a device which makes it possible to extirpate tumours hitherto so inaccessible that their attempted removal would have been regarded as foolhardy in the extreme . . . . Electro-surgery at least permits us to-day to remove certain brain tumours from situations and under circumstances which a year ago—indeed six months ago—I would not have thought possible.

A further article concerning the more extensive use of electrosurgical

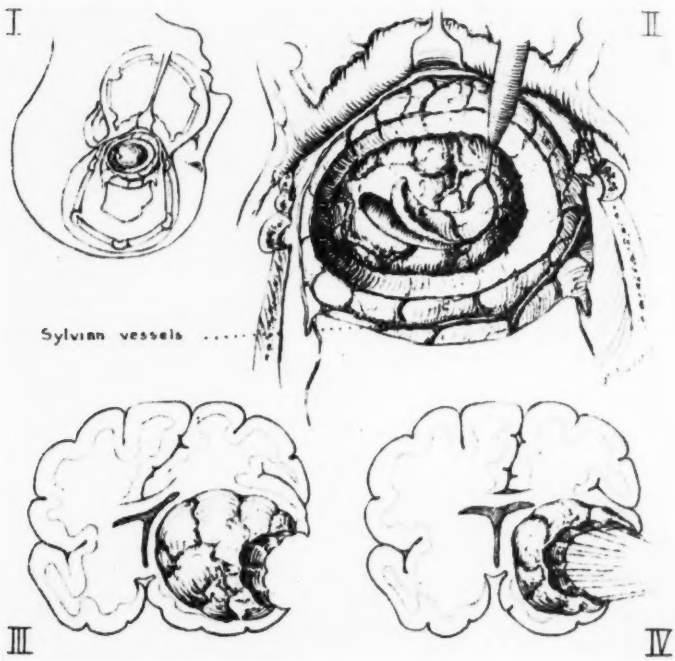


FIG. 12. Successive stages in the extirpation of a vascular meningioma of the left temporal region by means of "scalloping" and eventual removal of tumor shell.[25]

methods in intracranial surgery was published in collaboration with Dr. Bovie in 1928.[25] Here Cushing gave descriptions and illustrations of a variety of uses for the new apparatus for different types of brain tumors in various situations (Fig. 12). He called attention to the use of suction in keeping the field dry at the point where electrocoagulation was being applied, and

pointed out the value of suction in picking up deeply situated bleeding arteries so that they could be grasped with forceps and coagulated.

One other communication concerning a specific variety of meningioma must be mentioned. This was Cushing's paper,[29] published in 1929 in collaboration with Louise Eisenhardt, on the tumors of this category arising from the tuberculum sellae. The importance of the contribution lies in calling attention to a diagnostic symptom-complex for a specific lesion so that a more intelligent operative attack could be planned. To use Cushing's own phraseology,

> Not only is it essential that the presence of a tumor and of its precise location be reasonably assured before it is attacked, but it should be possible to make at least a presumptive guess as to its histologic nature and likelihood of recurrence, for these things will greatly influence the surgical procedure. The goal, in short, is to recognize the peculiar manifestations of a particular kind of tumor in a particular region at the earliest possible stage of the process in order that an operation may be undertaken under the most favorable auspices.

From this series of tumors, Cushing could conclude that the presence of "primary optic atrophy and bitemporal field defects combined with a normal sella turcica in a middle aged person" was practically diagnostic of a meningioma arising from the tuberculum sellae. In addition to the diagnostic criteria, Cushing's highly successful operative experience in a large proportion of his 15 patients having this type of lesion was detailed.

In 1932, Harvey Cushing ended his surgical career upon his retirement from the Moseley Professorship of the Harvard Medical School and from his position as Surgeon-in-Chief to the Peter Bent Brigham Hospital in Boston. On two occasions during the previous year he presented the mortality statistics pertaining to his large series of verified brain tumors, a grand total of 2,023 patients, 1,870 of whom were operated upon.[27,28] There were 382 postoperative deaths, namely, patients who died in the hospital from any cause whatever after operation, giving a case mortality of 20.4 per cent. This series, of course, included all of Dr. Cushing's brain tumor patients, starting with his earliest experiences in Baltimore in 1902. When the extremely high mortality of the early years is considered, it is indeed amazing that his total mortality was as low as it proved to be. As a contrast to the figures for the whole series, Cushing included the statistics for the three years previous to the communication. These showed that 412 patients with verified intracranial growths had been operated upon during that time, with 55 postoperative deaths, a case mortality of 13.3 per cent. It is quite probable that these figures stand today, more than ten years after their publication, as a mark which as yet has been unattained by his successors in this branch of surgery.

Amazing and highly successful as was Cushing's experience with brain tumors in general, his achievements in respect to a single large group of tumors, the meningiomas, was, if anything, even more striking. It is not within the province of this review to attempt a summary of his last comprehensive and monumental book devoted to these tumors, which appeared

with the collaboration of Dr. Eisenhardt in 1938.[30] The work is a vast storehouse of information, which was gathered by Dr. Cushing, his patients and his co-workers over the course of thirty-odd years, and ranks as one of his major contributions to neurological surgery. It must suffice to say that so far as the surgical statistics and end results are concerned, Cushing's operative ability with the difficult and often extremely hazardous procedures in removing these growths was phenomenal. In all, 281 of the 295 intracranial meningiomas were operated upon, with only 55 postoperative deaths, a case mortality of 19.6 per cent. These figures, just as the ones for his whole tumor series, go back to the early days of brain tumor surgery, when mortality was extreme. A contrast, therefore, should be made with his last five year period, from 1927 to 1932 (after the advent of electrosurgery). During this period, 118 patients were operated upon, with 14 postoperative deaths, an 11.8 per cent case mortality. In addition, his records showed that no less than 172 patients at the time of writing had survived from five to twenty-seven years.*

Sufficient has been said to make it clear that Harvey Cushing's experimental, pathological, clinical and technical contributions to neurological surgery were of such a character and of such extent as to make him the outstanding figure of his generation, surpassed in priority and in pioneering only by Sir Victor Horsley. Other very real but less tangible contributions could be enumerated, but time and space do not serve. It should at least be mentioned, however, that he continually preached the gospel, first intimated by von Bergmann, that neurosurgeons should be capable of making their own diagnoses by familiarizing themselves with the essentials of neurology, to which should be added certain features of ophthalmology. He exemplified in all his daily doings the value of patience under trying circumstances, meticulous care in everything that pertained to the welfare of those under his care and the attention to preoperative and postoperative details. His complete records of patients, together with his own exact as well as artistic operative sketches, are a model to all. All these things, as well as his wide experience aided in his almost uncanny neurosurgical judgment. Again, he organized the first society of neurological surgeons, in order that those interested in this new specialty might visit each other's clinics and thus gain added knowledge of the subject by observation and mutual discussion. Finally, by attracting to his clinic large numbers of young men from this and many other countries, he may be said truly to have established a school of neurosurgery throughout the world.

---

* In connection with the follow-up records on these patients, it should be noted that shortly after Dr. Cushing's removal to New Haven in 1933, he established the Brain Tumor Registry, with his longtime associate, Dr. Louise Eisenhardt, in charge. The Registry has been of the utmost help, not only in following groups of Cushing's patients but in making pathological diagnoses from microscopic sections of unusual or confusing tumors submitted by neurosurgeons throughout the country.

REFERENCES

1. Bailey, P., and Cushing, H. A classification of the tumors of the glioma group on a histogenetic basis with a correlated study of prognosis. *Philadelphia, London & Montreal: J. B. Lippincott Co.*, 1926, 175 pp.
2. Cushing, H. A method of total extirpation of the Gasserian ganglion for trigeminal neuralgia. By a route through the temporal fossa and beneath the middle meningeal artery. *J. Amer. med. Ass.*, 1900, *34:* 1035–1041.
3. Cushing, H. Concerning a definite regulatory mechanism of the vaso-motor centre which controls blood pressure during cerebral compression. *Johns Hopk. Hosp. Bull.*, 1901, *12:* 290–292.
4. Cushing, H. On routine determinations of arterial tension in operating room and clinic. *Boston med. surg. J.*, 1903, *148:* 250–256.
5. Cushing, H. Pneumatic tourniquets: with especial reference to their use in craniotomies. *Med. News, N. Y.*, 1904, *84:* 577–580.
6. Cushing, H. The special field of neurological surgery. *Cleveland med. J.*, 1905, *4:* 1–25. Also: *Johns Hopk. Hosp. Bull.*, 1905, *16:* 77–87.
7. Cushing, H. Concerning surgical intervention for the intracranial hemorrhages of the new-born. *Amer. J. med. Sci.*, 1905, n.s. *130:* 563–581.
8. Cushing, H. The establishment of cerebral hernia as a decompressive measure for inaccessible brain tumors; with the description of intermuscular methods of making the bone defect in temporal and occipital regions. *Surg. Gynec. Obstet.*, 1905, *1:* 297–314.
9. Cushing, H. Technical methods of performing certain cranial operations. *Interst. med. J.*, 1908, *15:* 171–187.
10. Cushing, H. Surgery of the head. In: *Surgery, its principles and practice.* W. W. Keen, Ed. Philadelphia: W. B. Saunders Co., 1908, *3:* 17–276.
11. Cushing, H. Some principles of cerebral surgery. *J. Amer. med. Ass.*, 1909, *52:* 184–192.
12. Cushing, H. A method of combining exploration and decompression for cerebral tumors which prove to be inoperable. *Trans. Amer. surg. Ass.*, 1909, *27:* 565–572. Also: *Surg. Gynec. Obstet.*, 1909, *9:* 1–15.
13. Cushing, H. Cases of cerebellar tumor, with the statistics of thirty operations. *Interst. med. J.*, 1909, *16:* 607–613.
14. Cushing, H. Recent observations on tumours of the brain and their surgical treatment. *Lancet*, 1910, *1:* 90–94.
15. Cushing, H. The special field of neurological surgery: five years later. *Johns Hopk. Hosp. Bull.*, 1910, *21:* 325–339. Also: *Cleveland med. J.*, 1910, *9:* 827–863.
16. Cushing, H. The control of bleeding in operations for brain tumors. With the description of silver "clips" for the occlusion of vessels inaccessible to the ligature. *Ann. Surg.*, 1911, *54:* 1–19. Also: *Trans. Amer. surg. Ass.*, 1911, *29:* 389–410.
17. Cushing, H. The pituitary body and its disorders. Clinical states produced by disorders of the hypophysis cerebri. An amplification of the Harvey Lecture for December, 1910. *Philadelphia & London: J. B. Lippincott Co.*, 1912, 341 pp.
18. Cushing, H. Concerning the results of operations for brain tumor. *J. Amer. med. Ass.*, 1915, *64:* 189–195.
19. Cushing, H. Tumors of the nervus acusticus and the syndrome of the cerebellopontile angle. *Philadelphia & London: W. B. Saunders Co.*, 1917, 296 pp.
20. Cushing, H. Notes on penetrating wounds of the brain. *Brit. med. J.*, 1918, *1:* 221–226.
21. Cushing, H. A study of a series of wounds involving the brain and its enveloping structures. *Brit. J. Surg.*, 1918, *5:* 558–684.
22. Cushing, H. The major trigeminal neuralgias and their surgical treatment based on experiences with 332 Gasserian operations. First paper. The varieties of facial neuralgia. *Amer. J. med. Sci.*, 1920, *160:* 157–184.
23. Cushing, H. The meningiomas (dural endotheliomas): their source, and favoured seats of origin. *Brain*, 1922, *45:* 282–316. Also: *West London med. J.*, 1922, *27:* 109–143.
24. Cushing, H. The meningiomas arising from the olfactory groove and their removal by the aid of electro-surgery. *Glasgow: Jackson, Wylie & Co., Publishers to the University*, 1927, 53 pp. Also (in part): *Lancet*, 1927, *1:* 1329–1339.
25. Cushing, H. Electro-surgery as an aid to the removal of intracranial tumors. With a preliminary note on a new surgical-current generator by W. T. Bovie, Ph.D., Chicago. *Surg. Gynec. Obstet.*, 1928, *47:* 751–784.

26. Cushing, H. Experiences with the cerebellar astrocytomas. A critical review of seventy-six cases. *Surg. Gynec. Obstet.*, 1931, *52:* 129–204.
27. Cushing, H. The surgical mortality percentages pertaining to a series of two thousand verified intracranial tumors. Standards of computation. *Trans. Amer. neurol. Ass.*, 1931, 456–463. Also: *Arch. Neurol. Psychiat., Chicago*, 1932, *27:* 1273–1280.
28. Cushing, H. Intracranial tumours. Notes upon a series of two thousand verified cases with surgical-mortality percentages pertaining thereto. *Springfield, Ill.: Charles C Thomas*, 1932, 150 pp.
29. Cushing, H., and Eisenhardt, L. Meningiomas arising from the tuberculum sellae: with the syndrome of primary optic atrophy and bitemporal field defects combined with a normal sella turcica in a middle-aged person. *Trans. Sect. Ophthal. Amer. med. Ass.*, 1928, 322–408. Also: *Arch. Ophthal., Chicago*, 1929, *1:* 1–41; 168–205.
30. Cushing, H., and Eisenhardt, L. Meningiomas. Their classification, regional behaviour, life history, and surgical end results. *Springfield, Ill.: Charles C Thomas*, 1938, 785 pp.
31. Henderson, W. R. The pituitary adenomata. A follow-up study of the surgical results in 338 cases (Dr. Harvey Cushing's series). *Brit. J. Surg.*, 1939, *26:* 811–921.
32. Horsley, V. On the technique of operations on the central nervous system. *Brit. med. J.*, 1906, *2:* 411–423.
33. Sänger, A. Ueber die Palliativoperation des Schädels bei inoperablen Hirntumoren. *Verh. dtsch. Ges. Chir.*, 1902, *31:* 158–162.
34. Spiller, W. G., and Frazier, C. H. The division of the sensory root of the trigeminus for the relief of tic douloureaux. *Univ. Pa. med. Bull.*, 1901, *14:* 341–352.

THE USE OF PRODUCTS PREPARED FROM HUMAN FIBRINOGEN AND HUMAN THROMBIN IN NEUROSURGERY

FIBRIN FOAMS AS HEMOSTATIC AGENTS; FIBRIN FILMS IN REPAIR OF DURAL DEFECTS AND IN PREVENTION OF MENINGOCEREBRAL ADHESIONS*

FRANC D. INGRAHAM, M.D., AND ORVILLE T. BAILEY, M.D.
Departments of Physical Chemistry, Surgery and Pathology, Harvard Medical School, and the Surgical Services of The Children's Hospital and the Peter Bent Brigham Hospital, Boston, Massachusetts

(Received for publication December 17, 1943)

INTRODUCTION

DURING THE PAST FORTY YEARS neurosurgical operations have developed from hazardous and rarely successful *tours de force* to well standardized and relatively safe procedures. Many of the major contributions to this rapid development are due to the investigations and teaching of Harvey Cushing. By adapting techniques of general surgery to the particular requirements of the neurosurgeon and by the development of new techniques to meet problems not encountered in other fields of surgery his work was a definitive influence in modern neurosurgery.

Two of the many groups of problems which still await satisfactory solution are those connected with hemostasis and those related to the prevention of meningocerebral adhesions. For progress in each of these directions, new materials are needed to supplement or supplant those now at hand.

Substances which may be applicable to both these groups of problems have recently been prepared on a large scale by the Department of Physical Chemistry at the Harvard Medical School by the fractionation of human blood plasma.[2] Of particular interest in the technique of neurosurgery are two materials derived from the proteins connected with the clotting mechanism.[4] In addition to whatever advantage may accrue from materials of human origin, they are susceptible to a wide variation by small alterations in the conditions of their preparation. Of these, one is a spongy substance, which has been designated as "fibrin foam." Another is a film of fibrin which is pliable, elastic and translucent. In this paper, we wish to describe experimental, clinical and pathological studies on the use of fibrin foam as a hemostatic agent and of fibrin film as a dural substitute and in the prevention of meningocerebral adhesions.

* This paper is No. 27 in the series "Studies on Plasma Proteins" from the Department of Physical Chemistry of the Harvard Medical School, Boston, Mass. This work, supported by grants from the Rockefeller Foundation and from funds of Harvard University, was aided early in 1941 by grants from the Committee on Medicine of the National Research Council. Since August, 1941, it has been carried out under contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University, employing blood collected by the American Red Cross.

PART ONE—FIBRIN FOAMS

Bleeding from medium sized vessels in the central nervous system and its coverings can be satisfactorily managed in most instances by the use of the conventional methods of hemostasis, such as silver clips and electrocoagulation. The oozing from vessels on the surface of the dura and in the substance of the brain and spinal cord is less easily controlled by these means. Pressure from cotton patties soaked in warm or hot saline solution is often effective while pressure is maintained. When the patties are removed, the oozing will often begin again and the procedure may have to be repeated several times. This occupies a considerable amount of time and may prolong the operative procedure; it occasionally fails to effect perfect hemostasis. The introduction of muscle by Cushing in 1911[3] provided an effective absorbable agent for hemostasis in such locations. However, muscle used in this way has certain shortcomings. It is not always immediately available in sufficient quantities and it causes an appreciable tissue reaction. Grey[8] and Harvey[9] prepared fibrin tampons from animal and human fibrin. These proved good hemostatic agents and caused less reaction than muscle in similar locations but have never become widely used in human neurosurgery. Numerous experiments have been performed with thrombin of animal origin as a hemostatic agent in neurosurgery, at times with considerable success.[16] A further step in the development of an absorbable hemostatic agent was made in 1943 by Putnam.[15] He used a soluble cellulose soaked in thrombin solution, the thrombin being of either animal or human origin. This soluble cellulose was prepared by the oxidation of cellulose by nitrogen dioxide.[17,18] Putnam's results in neurosurgical operations were satisfactory. Histological studies of the tissue reaction elicited by this material were made by Frantz.[7] The cellulose was very rapidly absorbed and produced minimal tissue reaction.

It would seem that an absorbable hemostatic agent prepared from materials entirely of human origin might have significant advantages. This has been done by Bering.[1]

The fibrin foams are prepared from human fibrinogen and human thrombin. In the dry state the foams are composed of dense strands of fibrin fibers with air spaces which may easily be seen with the naked eye. The fibrin foam is dull, porous and slightly brittle.[1]

As supplied at present, the fibrin foams are packaged in the dry state. Along with them is a small vial containing dried human thrombin. At the operating table, the thrombin is dissolved in 50 cc. of physiological saline solution. The powder is rapidly dissolved, solution being complete in less than one minute if there is vigorous stirring. Portions of fibrin foam are then placed in the thrombin solution; pieces of various sizes and shapes are chosen so that they will be ready for all circumstances likely to arise in the course of the operation. If unexpected difficulties should arise, an additional amount of foam and thrombin could be readily prepared.

As the foam becomes saturated with the thrombin there is a moderate amount of spontaneous shrinkage. The porosity of the fibrin matrix allows for swift penetration of the thrombin solution to all parts of the mass.

LIBRARY
WEST VIRGINIA UNIVERSITY

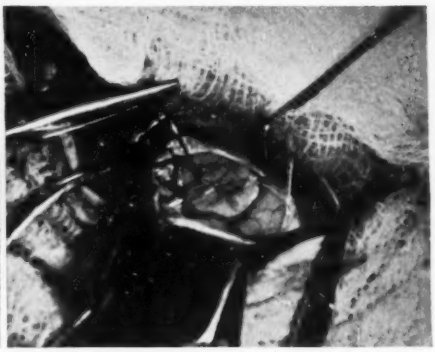


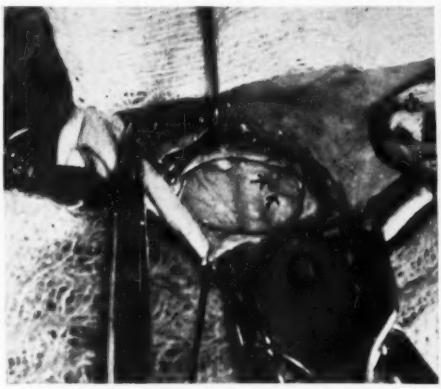
FIG. 1 (*left*). Operative field in the brain of an experimental monkey. Foam has been placed on the intact cortex.

FIG. 2 (*right*). Technique of multiple needle punctures of cerebral cortex.

ANIMAL EXPERIMENTS

In order to determine the local effect of fibrin foam on tissues, a series of experiments was set up in large monkeys (*Macaca mulatta*). The operative procedure was as follows:

The animals were anesthetized with nembutal administered intraperitoneally, the head shaved and the scalp prepared with alcohol and zephiran. A mid-line incision was then made in the scalp and the temporal muscles incised. The parietal bone was penetrated with a burr and a defect, roughly 2.5 × 4 cm. was made in it with rongeurs. In different operations, the following variations in intracranial procedure were introduced. Foam soaked in thrombin was placed on the intact cortex (Fig. 1), on the cortex after it had been traumatized by multiple needle wounds (with hemorrhage) (Fig. 2) and at other times pieces of foam roughly



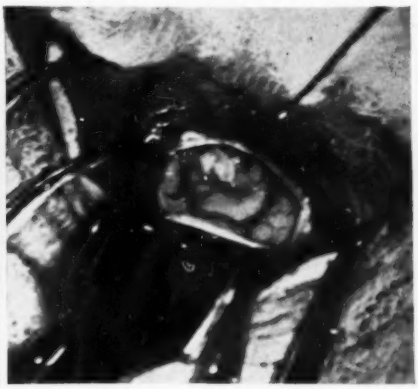


FIG. 3 (*left*). Cortex of monkey showing amount of tissue removed. Single arrow points to the tissue removed; double arrow, to the defect left in the cerebrum.

FIG. 4 (*right*). Foam implanted in a defect similar to that shown in Fig. 3.

4×4×6 mm. were implanted in the substance of the parietal lobe at a depth of 3 mm. beneath the surface of the arachnoid. In other instances a piece of cerebral cortex was removed (Fig. 3) and replaced by foam (Fig. 4). Each of the variants was repeated with the alteration that 50 mg. of sulfadiazine were sprinkled on the surface of the wound before closure. Again, each of the procedures was carried out with penicillin placed in the wound after the foam had been implanted. Soluble cellulose in combination with thrombin was introduced with the same variations on the left side in a series of animals and fibrin foam with identical operative procedures was placed on the right side. No physiological changes were observed as a result of these implantations. The animals were sacrified with an overdose of nembutal at intervals from 24 hours to 3 months.

Immediately after sacrifice, the heads of the monkeys were removed and the mandibles, maxillae and skin were cut away. The skulls were then fixed in ten per cent formalin. After fixation for ten days, dissection was carried out so as to preserve the relationships of the meninges and the underlying cerebral tissue. This was accomplished by trimming the skull away bit by bit with rongeurs so that the dura was not torn and the site of operation disturbed as little as possible. The operative field and underlying cortex were then cut in thin blocks and refixed in ten per cent formalin. The blocks were embedded in paraffin and stained with hematoxylin and eosin.

Pieces of fibrin foam which had not been implanted in animals were fixed and stained by the same technique. In these, the fibrin foam appeared as a wide-meshed network of fibers considerably broader than the fibers of a blood clot but with the same staining reactions. The interstices were entirely clear.

In the monkey autopsied 24 hours after the implantation of the foam, the interstices of the foam were filled with blood clot. The delicate strands of the fibrin of the blood clot could be clearly differentiated from the coarser, more homogeneous fibers of the implanted material. A small number of polymorphonuclear leucocytes and mononuclear cells were seen in some portions. The amount of cellular infiltration was so small that it was difficult to be sure how much of the cellular reaction was due to the foam and how much was a part of the blood clot. In the monkeys sacrificed at the end of one week the foam had largely disappeared. About the residual fragments there were a few polymorphonuclear leucocytes and some mononuclear cells but the cellular reaction was, in each instance, very slight. At this time the small bits of foam remaining had become compact and the fibrillar structure was largely obliterated. There was also a very slight proliferation of connective tissue about the bits of foam. At the end of three weeks, no fragments of foam could be identified. When pieces of fibrin foam had been introduced directly into the substance of cerebral cortex, the implanted material disappeared at least as rapidly as when placed on the meninges and possibly somewhat more rapidly. The small amount of gliosis, which was the only trace of the former presence of the foam, did not appear to be in excess of that which might be accounted for by the trauma of the operative procedure.

As indicated in a preceding paragraph, experiments were set up to compare tissue reactions to soluble cellulose soaked in thrombin and to fibrin

foam immersed in thrombin solution. The tissue reactions to soluble cellulose in our series of monkeys agreed with those described by Frantz.[7] In two monkeys, adhesions were present between the arachnoid and dura on the left side, where soluble cellulose had been implanted, but no adhesions were found on the right side, where fibrin foam had been used. Because of the variation inherent in the reactions to the operative procedure itself we have not regarded this as a significant difference. The speed of reaction and extent of tissue proliferation was almost identical with the two substances tested.

The addition of sulfadiazine to the experimental wounds containing fibrin foam produced no recognizable change in the speed of absorption of the foam or in the nature of the cellular response to its presence. This is in agreement with previous studies on the tissue reaction in neurosurgical wounds.[10]

A similar comparison was made between fibrin foam in wounds without bactericidal agents and fibrin foam in wounds to which penicillin had been added. The speed of absorption and the nature of the tissue reaction was not altered by the presence of the penicillin.

CLINICAL STUDIES

When the fractions of human blood plasma were first made available, human thrombin solution was applied to bleeding points in the course of several cranial and spinal operations by using ordinary cotton patties or dental rolls. This method appeared to be only moderately effective since the bleeding, although controlled temporarily, started up again as soon as the cotton was removed. It is of interest that on one occasion the thrombin solution reached the lateral ventricle without apparent ill effect.

It seemed to us that the development of an absorbable agent which might be used with the thrombin solution would be of considerable advantage. Since fibrin foam has been available, we have used it in 95 neurosurgical operations and have had an opportunity to recover the material at reoperation or autopsy in 18 instances. The conditions for which these operations have been undertaken have covered a considerable range (Table I), and the need for hemostasis has varied from being almost inconsequential, to dire emergency. The method of application has been essentially the same in all instances. The field has been dried as well as possible by suction, an appropriate sized piece of foam soaked in a saturated solution of human thrombin placed on the bleeding surface and held in position for several minutes with cotton patties or (in the case of a deep wound) lintene strips. The first experiences were limited to those operations in which control of bleeding was extremely difficult and not amenable to treatment by application of muscle. For example, one such instance was in dealing with a blood vessel malformation exposed in the course of an operation for focal epilepsy. The foam proved to be strikingly effective even when such large venous channels had been opened. The same result has been achieved in dealing with openings in dural sinuses.

The use of foam was then extended to simple types of bleeding, for example, oozing from the surface of the brain or the outer surface of the dura (Figs. 5 and 6). Under such circumstances, the application of a very small piece of the material stopped oozing instantly and thus saved an appreciable amount of time. During closure of the dura at the end of an extensive operation the all too familiar venous bleeding which may start up from the dura under the margin of the bone has been controlled simply and promptly by pressing a small piece of foam between the bone and the dura. In this series of patients, the foam has been used in amounts varying from a fragment 2 or 3 mm. in diameter to a mass larger than a golf ball placed in a tumor bed. In such instances as the latter, most of the foam has usually been removed piecemeal before closure. A mass of this size has occasionally been left in place and there is no reason why it should not be left whenever necessary.

A more detailed example of the use of foam is given in the following case history:

K.G. CH #238090. A well developed and nourished 12 year old school girl was admitted with complaint of headache and vomiting. Four years previously she had had an incomplete removal of a cystic astrocytoma of the right cerebellar hemisphere. Physical examination showed high grade papilledema, ataxia; in short, the classical clinical syndrome of cerebellar tumor. At operation, the muscles were found to be densely adherent to the scarred cerebellum and there was finally exposed a large tumor mass replacing almost the entire right hemisphere. This mass was gradually freed from the surrounding cerebellar tissue, mobilized, and removed *en masse*. As the tumor was delivered there was free bleeding from its bed. Foam corresponding in aggregate to the size of the tumor was immediately introduced into the depths of the wound. This was held in place by lintene strips which were shortly removed, as was about three quarters of the foam. This left the field quite dry and closure was promptly carried out. Recovery was uneventful.

The general distribution of the cases in this series is shown by Table I.

TABLE I

Tumor, intracranial or intraspinal	42
Lead encephalopathy	3
Congenital anomaly (Arnold-Chiari, etc.)	21
Depressed fracture	2
Jacksonian epilepsy	7
Subdural hematoma	7
Herniated nucleus pulposus	3
Miscellaneous	10
Total	95

In studying the specimens removed at secondary operations or at autopsy on human patients, the histological technique was somewhat different from that used in the animal experiments. The tissues were fixed in acetic Zenker's fluid, embedded in paraffin, and stained with phloxine and methylene blue. With this technique, fibrin foams which were not implanted stained deep blue but otherwise had the same general characteristics described before. They appeared as networks of coarse fibers with clear interstices.

In the specimen obtained at the end of 14 hours (Fig. 7) the interstices were filled with blood clot. There was practically no detectable tissue reac-

FIG. 5. Oozing from the human dura and cerebral cortex in the course of a secondary exploration.

FIG. 6. Control of bleeding from the human dura and cerebral cortex with fibrin foam.

tion. It should be borne in mind that this patient, who had a radical removal of a pituitary adenoma, was rapidly failing during the 14 hours that the foam was in place. For this reason, the tissue reaction may have been less than it would have been had the patient been in good condition during the same period of time. The next specimen obtained was at the end of three days. In

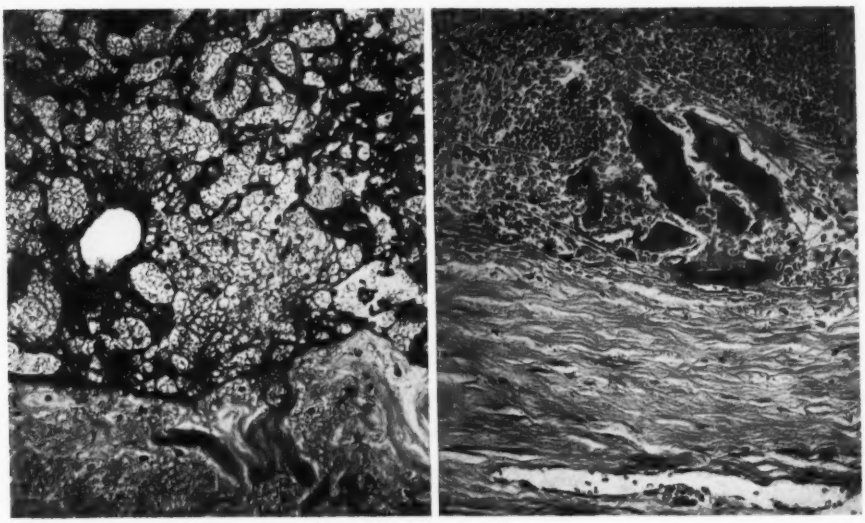


FIG. 7 (*left*). Photomicrograph of fibrin foam left on the surface of the human dura 14 hours previously. The coarse strands of the foam contrast clearly with the very delicate fibrin strands of the clotted blood in the interstices of the foam.

FIG. 8 (*right*). Fibrin foam placed on the human dura 6 days previously. Most of the foam has been absorbed and that which remains has become compact.

this specimen, a large portion of the foam had disappeared. That which remained was more compact than unimplanted foam but it still retained fibrillar structure. In the zone where the foam came in contact with living tissues, there was a narrow margin which took the eosin stain while all the rest of the foam retained the deep blue color of unimplanted foam. About the fragments there were a few polymorphonuclear leucocytes, mononuclear cells and some lymphocytes. Some of the cells contained bits of homogeneous material which took the eosin stain. These were regarded as bits of foam which were in the process of removal by phagocytosis. Giant cells were not encountered. At longer intervals the foam had almost entirely disappeared. Fig. 8 shows a specimen at the end of 6 days. There were a few fragments of foam which were microscopic in size although considerable quantities had been left in place at the time of operation. No fragments of foam were identified in a specimen obtained after 9 days (Fig. 9). In the specimen at 19 days (Fig. 10) the minute fragment of foam in the illustration was the only one

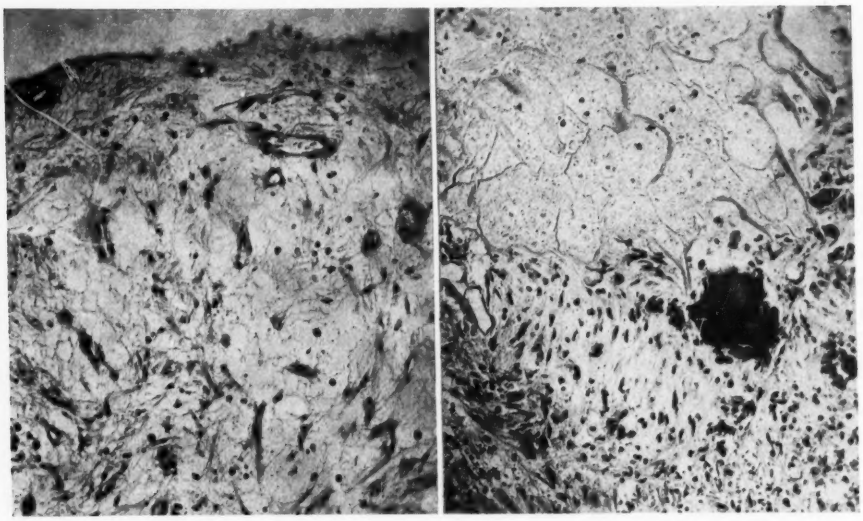


FIG. 9 (*left*). An organized blood clot at the site of implantation of foam in a patient 9 days previously. No residual foam is seen.

FIG. 10 (*right*). This minute fragment of foam was the only remnant found 19 days after a large amount had been implanted on the dura of a patient.

found in the specimen. At longer intervals none at all was present. There was one specimen of meninges and cerebral cortex obtained at 81 days after the implantation of foam. In this specimen, there was no residual foam and no tissue reaction in excess of that which would be expected from the operative procedure itself.

COMMENT

The development of fibrin foam with thrombin solution has introduced a new absorbable agent for hemostasis in surgery. Our experience has been wholly confined to its use in operations on the central nervous system. Fibrin foam has an *a priori* recommendation in its development entirely from proteins of human origin. Of how much practical importance this may prove eventually, experience is as yet inadequate to ascertain.

Aside from its theoretical acceptability, fibrin foam as now prepared has proved a most effective hemostatic agent in neurosurgical practice. Its most obvious sphere of usefulness is that of the control of oozing from small vessels. The use of foam has materially shortened many neurosurgical operations because the bleeding from the dura, from beneath the edges of the bone flap and from the spinal veins can be quickly brought under control. More important, however, is the fact that fibrin foam adequately controls the oozing from the beds of tumors. This permits the removal of neoplasms *en bloc* which might have had to be removed piecemeal or at several operations if this material were not available.

Another field in which the fibrin foams have proved of great value is in the control of bleeding from large venous channels. When there is oozing from large superficial cerebral veins, especially those entering the mid-portion of the superior longitudinal sinus, ligation is apt to be followed by cerebral softening. Such oozing may be controlled by the use of foam. It is also possible to stop bleeding from the superior longitudinal sinus or other dural sinuses by the use of a good sized piece of foam placed firmly against the sinus. The foam has also proved invaluable in dealing with blood vessel malformations of the cerebrum, lesions in which the bleeding is well known to be difficult to control by conventional measures. In these situations, the fibrin foam is not merely an agent to shorten neurosurgical procedures, but has succeeded where other agents have failed. Fibrin foam can hardly be expected to control bleeding from large arteries, which is best managed by silver clips.

The histological studies, both in man and in experimental animals, indicate that the foam is rapidly absorbed with a minimal, even negligible tissue reaction. In view of this, large pieces may be left if the occasion demands.

We have used fibrin foam clinically and experimentally in conjunction with such bactericidal agents as sulfadiazine and penicillin. The evidence indicates that no change in the properties of the foam or in the tissue reactions occurs under such circumstances.

PART II—FIBRIN FILMS

A suitable substitute for normal human dura mater is highly desirable for two primary reasons: first, the dura may have to be removed because of its involvement in a disease process; and second, the dura may be injured with or without damage to the underlying nervous tissue. In the neurosurgery of civilian life, the former need is the greater one; dura invaded by tumor has been removed routinely and replaced by one of a variety of materials with more or less satisfactory results. The needs for dural substitutes in the craniocerebral injuries of warfare are more largely those requiring an innocuous substance to provide protection to the nervous system during healing.

The literature dealing with dural substitutes with special reference to meningocerebral adhesions has been admirably reviewed by Pudenz and Odom[14] in connection with their own studies of the problem. They have described in detail the formation of the meningocerebral cicatrix and discuss its role in causing posttraumatic convulsions. The observations of Foerster and Penfield[6] in 1930 and additional studies of Penfield[12,13] since that time offer convincing evidence that meningeal ingrowth of the cerebral wound is the most important factor in producing posttraumatic convulsions.

In order to meet these needs for a protective layer which might be easily available, numerous materials have been studied in the laboratory and have been used clinically. Fascia lata, dural transplants, preserved dura, fat, periosteum, amniotic membrane, Cargile membrane, numerous metal foils

(gold, silver, aluminum, tantalum, etc.), cellophane, and rubber tissue have all been used with varying results. The conclusion reached by Pudenz and Odom[14] after their extensive studies summarizes the situation clearly. They state that although some of the materials tested by them show promise, "none can be considered as having offered a solution to the problem."

The desirability of long time controls in a study of this problem is so obvious as to need no special emphasis. Because a dural substitute is critically needed in dealing with the craniocerebral injuries of the war, observations on the use of fibrin film developed in the Department of Physical Chemistry at Harvard Medical School are presented at this time.

The fibrin films which have been used in these experimental and clinical investigations are prepared in sheets of various sizes and thicknesses. They are composed of two parts; one part protein and the other a plasticizing agent.[5] The protein part, which makes up from 20 to 60 per cent of the films by weight, is at least 90 per cent fibrin. At the time the films are prepared, the remainder is composed of glycerol. However, the immersion of the films in water or saline removes the glycerol and the water which the film takes up should be regarded as the final plasticizer under these conditions. The films are smooth, translucent, uniform sheets with a considerable amount of elasticity. They are sufficiently strong to be sutured without tearing and can be easily trimmed to fit the dural defect. While the films are prepared in flat sheets, their elasticity allows them to be fitted with ease to rounded or irregular contours. After several days *in situ* over the brain or spinal cord, the films have been seen at secondary operations to assume the contour of the cerebral cortex beneath and to retain this contour when removed. The rate of absorption of fibrin films in tissues has been studied by Morrison and Singer.[11]

ANIMAL EXPERIMENTS

In order to determine the reaction of the cerebral cortex to the fibrin films, craniotomies were done on 10 monkeys (*Macaca mulatta*). Unusually large animals (average weight 8 kg.) were selected so that generous openings could be made. The operative procedure was carried out as follows:

The scalp was shaved and cleansed with alcohol, followed by zephiran. A midline incision was then made in the scalp, which was retracted laterally and the temporal muscle incised. In six animals an osteoplastic bone flap was turned down on the right side while the bone was removed with rongeurs on the left. On both sides, the dura was replaced with fibrin film, the margins of the film lying under the cut edge of the dura without suture. The bone flap was replaced on the right, the temporal muscle was closed over the defect on the left, and the superficial tissues on both sides were sutured with black silk.

This procedure was repeated with the following variations:

(1) The cerebral cortex was traumatized by multiple needle wounds (10–25) penetrating the cerebral cortex for at least 2 mm. These needle wounds were distributed so as to cause bleeding in every instance.

(2) Both experiments outlined above, i.e., exposure of the cerebral cortex with and without trauma, were repeated with the variation that 25–50 mg. of sulfadiazine were placed evenly over the exposed cortex beneath the film.

These animals were sacrificed by an overdose of nembutal after a period of observation varying from 24 hours to 6 months. During this time there was no physiological evidence of cortical irritation.

The same techniques for fixation, dissection and staining were used as in the case of the experiments with fibrin foams. When sections of the film were fixed and stained with hematoxylin and eosin without implantation of the film in an animal, the stained film was found to have a homogeneous structure which took the eosin stain. In the monkeys sacrificed up to one week

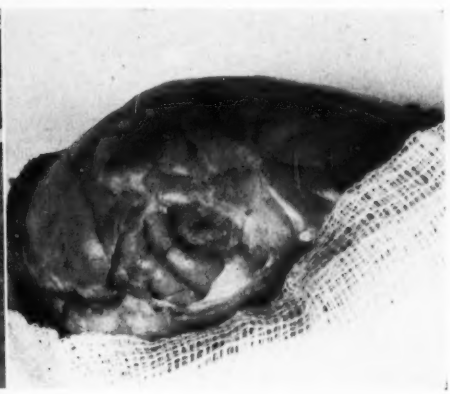


FIG. 11 (*left*). Low power photomicrograph of the brain and overlying meninges of a monkey 3 months after film had been placed over the intact cortex. At autopsy no meningocerebral adhesions were found and the clear subdural space is shown in the illustration. The film has been completely replaced by a neomembrane of fibrous tissue.

FIG. 12 (*right*). Brain of a monkey showing the area where the dura has been replaced by a fibrin film 6 months previously, the bone flap being retained. The dural defect is now covered by a thin, transparent neomembrane which is not adherent to the cerebral cortex. The neomembrane is still in place throughout the whole defect but is completely transparent.

after operation, the film had changed its appearance but little and there were only a few wandering cells about it. As time went on, the film became surrounded by a small amount of fibrous tissue from which it could be separated easily. In the monkeys allowed to survive more than a month, parts of the film could be seen broken up with some giant cells about the small isolated fragments. The end result was a layer of fibrous tissue about the same thickness as the original film. At the end of three months there was still a subdural space without adhesions between the dura and the arachnoid (Fig. 11). The monkey sacrificed at 6 months gave especially good material for study. On the side where the osteoplastic bone flap had been made, the layer covering the cerebral cortex was found to be composed of thin transparent fibrous tissue rather than film (Fig. 12). There were no adhesions between this layer and the underlying cerebral cortex, which appeared entirely normal (Fig. 13). On the opposite side of the same monkey, where the bone had been sacrificed, there were also no adhesions although the region in which the

layer of fibrous tissue replaced the film was closely connected to the overlying temporal muscle. Here again the subdural space was entirely free from adhesions (Fig. 14).

The incorporation of sulfadiazine in the wounds in which films were

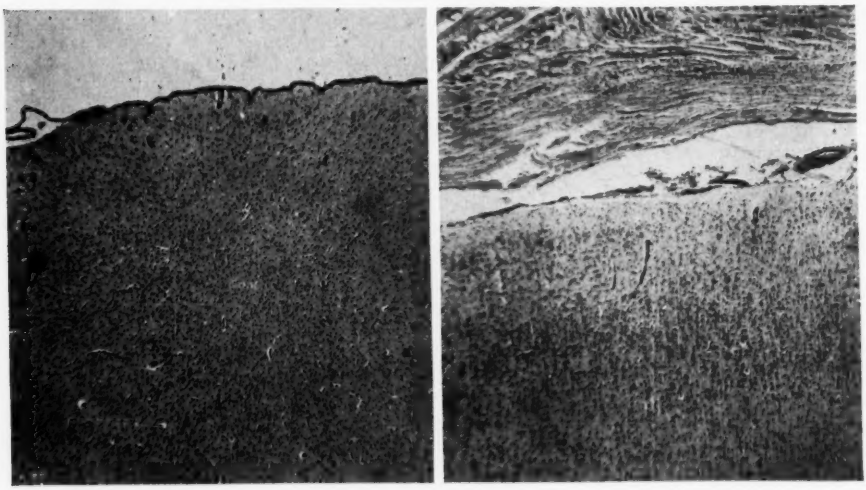


FIG. 13 (*left*). Low power photomicrograph of the cerebral cortex beneath the film shown in Fig. 12. The arachnoid is regular and the structure of the cerebral cortex is normal.

FIG. 14 (*right*). Photomicrograph of the brain and meninges of the opposite side of the monkey shown in Fig. 12. On this side a bony defect had been created. The cerebral cortex is well preserved and there are no adhesions between the dura and arachnoid. The film has been entirely replaced by a neomembrane of fibrous tissue which is adherent to the overlying muscle.

placed resulted in no change in the tissue reaction and did not have any detectable effect upon the films themselves.

CLINICAL STUDIES

As soon as preliminary animal experiments had been completed, the film was used as a dural substitute in patients. At first its use was limited to relatively hopeless situations or to operative procedures which were apt to be followed by reexploration. Altogether, the film has been used in 44 patients and recovered for study in 18 instances. The underlying pathology for which operation was undertaken in this group varies through a wide range, as shown in Table II.

TABLE II

Tumor, intracranial and intraspinal	25
Congenital anomaly	8
Lead encephalopathy	6
Compound fracture	2
Jacksonian epilepsy	3
Total	44

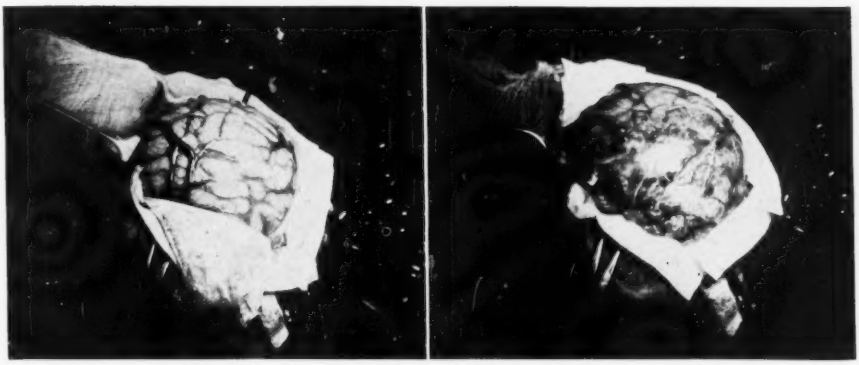


FIG. 15 (*left*). Right hemisphere of patient with severe lead encephalopathy exposed at operation. (Cerebrospinal fluid pressure 750 mm. of water.)

FIG. 16 (*right*). Fibrin film has been placed over the cortex exposed by retraction of the dura.

The exact conditions and the size of the dural defect or damage were quite variable.

In general, the film was used wherever dura had to be removed or when the cortex was left unprotected because of the retraction of normal dura as, for instance, in a decompression. In each instance the film was cut slightly larger than the defect and the edges passed underneath the cut margin of the dura. The use of a large piece of film to protect the cerebral cortex under markedly increased pressure in lead encephalopathy is shown in Figs. 15–20.

An example of its use in replacing dura infiltrated by tumor is given in the following case history:

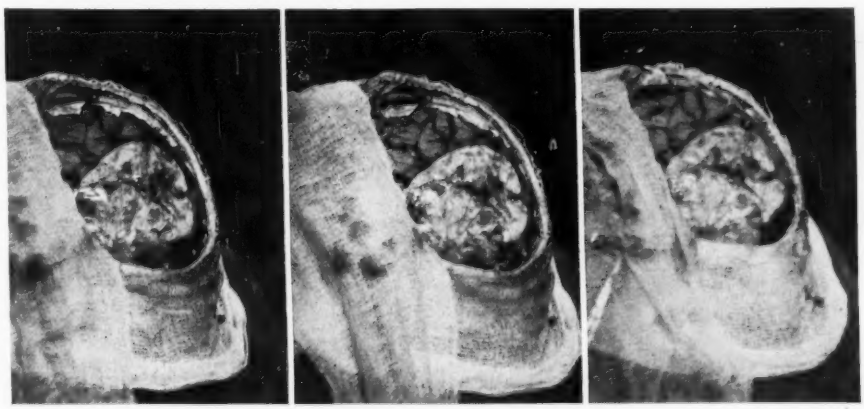


FIG. 17 (*left*). The operative field shown in Fig. 16 is reexposed after pressure had returned to normal 18 days later. The original fibrin film is still in place.

FIG. 18 (*center*). The film has been removed from the operative field shown in Fig. 17.

FIG. 19 (*right*). A new film has been placed over the cortex of the operative field shown in Fig. 18.

A.R. CH #278750. Age 5 4/12 years. A pale undernourished boy was admitted to the hospital in coma. At the age of 4 months he had fallen and had been unconscious for ten minutes. He had been slow in development and had been regarded as suffering from arrested hydrocephalus. He was not considered acutely ill until 2 months before admission when his gait became unsteady and his vision poor. One month before admission, he began to vomit and lost weight steadily, gradually sinking into coma.

Physical examination revealed a thin pale child with a rather large head. There was a soft prominence in the mid-parietal region as shown in Fig. 21. There was bilateral papilledema, ankle clonus and positive Babinski sign.

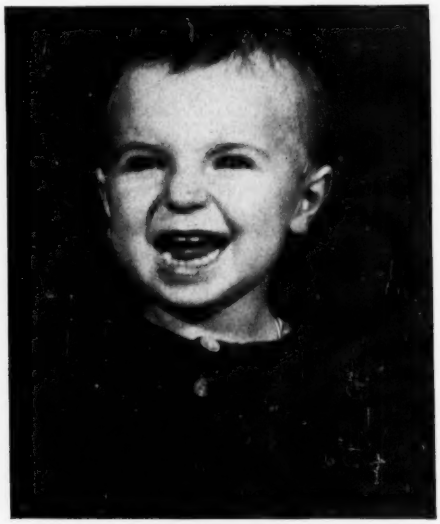


FIG. 20. Patient whose cortex is shown in Figs. 15–19, 6 months after operation. Large pieces of film have been left over the surface of both hemispheres. There have been no signs whatever of cortical irritation.

Roentgenograms showed separation of the coronal suture and irregular destruction of the right parietal bone. A lumbar puncture needle was passed through the coronal suture and brown mucilaginous material removed from the subdural space on both sides. The patient improved appreciably after this procedure, which was repeated daily until exploration was carried out. At this time, a right parietal scalp flap was turned down and a firm tumor extending through the bone exposed (Fig. 22).

The involved bone was removed, thus uncovering an extensive dural tumor (Fig. 23). The portion of tumor and dura available through this bony defect was excised and a large subdural collection of fluid evacuated. The cortex was covered with a layer of fibrin film and the scalp closed. Six days later the scalp flap was reflected and brain found to be protruding through the bony defect under increased tension. It was covered by the film (Fig. 24) which had conformed to the shape of the protruding brain. The film was removed (Fig. 25) without disturbing the cortex (Fig. 26). A bone flap was then turned down over a larger area and the dura at the peripheral portion of the bone flap was removed, together with a large amount of tumor. This larger area was then covered with film (Fig. 27) and the flap closed. The histological diagnosis was fibrosarcoma of the meninges. The use of the film made it possible to sacrifice a large amount of dura involved by the tumor. While all the tumor could not be removed and a permanent cure is not to be expected, marked immediate improvement has resulted from the operative procedure.

Those instances in which reexploration has made examination of the film possible have been of the greatest aid in evaluating fibrin film as a dural substitute. Film has been removed at operation or autopsy at intervals varying from 14 hours to 81 days after implantation. In no instance was the slightest evidence of an inflammatory reaction seen in the gross. The complete absence of adhesions has been very striking.

The films available for histological study were recovered at secondary operation or at autopsy in 10 patients. These films covered a time interval of 14 hours to 81 days after surgical implantation of the films. The films and

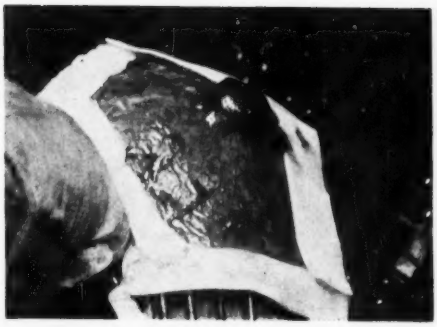


FIG. 22. The tumor in the patient A. R. has been exposed by reflection of the scalp.

FIG. 23. The tumor of the dura has been exposed by removal of the involved bone.

FIG. 24. Reexploration of patient A. R. 6 days after the dural defect had been covered by fibrin film.

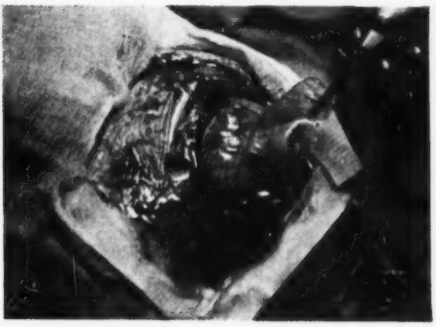


FIG. 25. The fibrin film shown in Fig. 24 has been partially removed. Note absence of adhesions between the film and the underlying cortex.

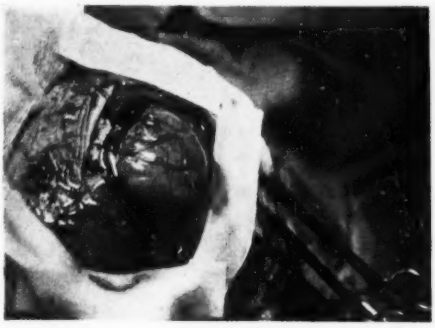


FIG. 26. Cortex of the patient A. R. shown in Fig. 25 after complete removal of the film. The surface of the arachnoid is entirely smooth.

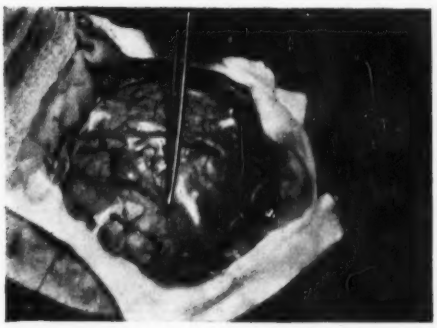


FIG. 27. Right hemisphere of patient A. R. after wide excision of dura and tumor. Another fibrin film has been placed over the dural defect.

FIG. 21. Patient A. R. after the intracranial pressure had been relieved by tapping the subdural cystic cavity. Note the prominence of the right parietal region.

surrounding tissues were fixed in Zenker's fluid, sectioned in paraffin and stained with phloxine and methylene blue. In addition, some sections were stained with hematoxylin and eosin and Van Gieson's stain. The film before implantation was, of course, identical with that used in the animal experiments. The tissue reactions both in extent and character were similar to those already described in the experimental animals (Fig. 28). The specimen obtained after 81 days (Fig. 29) showed the final stages of the break-up of the film with isolation of bits of it and the formation of a fibrous tissue layer. In the illustration the smooth surface of the specimen indicates clearly the lack of adhesions in response to its presence.

COMMENT

The need for caution in interpreting these results is too obvious to require emphasis. Histological material from animals with intracranial implantations of fibrin film with and without trauma, with and without sulfadiazine and penicillin over a period of more than 6 months has been carefully studied. Patients in whom fibrin film has been left in place over the cerebral cortex for a period of nine months have been followed closely and there has been no evidence of cortical irritation. It may be fairly concluded that as far as the present evidence goes, fibrin film is superior to other materials previously tested. As far as the authors know, there is no dural substitute now available

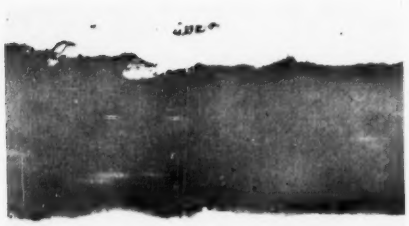


FIG. 28 (*left*). Photomicrograph of a fibrin film in place over the human cerebral cortex after 14 hours. Note the homogeneous structure and the lack of inflammatory response.

FIG. 29 (*right*). Fibrin film which had been in place in a patient for 81 days. Only small fragments of the original film remain. A neomembrane of fibrous tissue has been formed which is not adherent to the underlying cortex.

which produces as little local reaction and has at the same time the desirable attributes of fibrin film. These attributes are ease of handling (including possibility of fixation with sutures), translucence, flexibility, and adaptability to any contour.

SUMMARY

The human plasma fractionation studies of the Department of Physical Chemistry have made available considerable quantities of the plasma proteins connected with the clotting process. Two materials have been prepared from these proteins which have entirely different uses in neurosurgery.

Fibrin foam is an effective, absorbable hemostatic agent. It easily controls oozing from the dura, the beds of central nervous system tumors and the brain substance as well as venous bleeding from the spinal veins, superficial cerebral veins and the dural sinuses. Histological studies of experimental and human material have shown that the fibrin foam is rapidly absorbed and excites a minimal tissue reaction.

Fibrin films have been used as a dural substitute and in the prevention of meningocerebral adhesions. Patients followed up to 9 months have had entirely satisfactory results. These have paralleled observations in a series of monkeys.

Both fibrin foams and fibrin films may be used at the same time as sulfadiazine and penicillin without change in tissue reactions.

We wish to express our appreciation to Miss Edith Battey, R.N., for her assistance in this work.

REFERENCES

1. BERING, E. A., JR. Chemical, clinical and immunological studies on the products of human plasma fractionation. XXII. The development of fibrin foam as a hemostatic agent for use in conjunction with human thrombin. *J. clin. Invest.* (In press)
2. COHN, E. J., ONCLEY, J. L., STRONG, L. E., HUGHES, W. H., and ARMSTRONG, S. H., JR. Chemical, clinical and immunological studies on the products of human plasma fractionation. I. The characterization of the protein fractions of human plasma. *J. clin. Invest.* (In press)

3. Cushing, H. The control of bleeding in operations for brain tumors. With the description of silver "clips" for the occlusion of vessels inaccessible to the ligature. *Ann. Surg.*, 1911, *54:* 1–19.
4. Edsall, J. T., Ferry, R. M., and Armstrong, S. H., Jr. Chemical, clinical and immunological studies on the products of human plasma fractionation. XVI. Plasma proteins concerned in the blood coagulation mechanism. *J. clin. Invest.* (In press)
5. Ferry, J. D., and Morrison, P. R. Chemical, clinical and immunological studies on the products of human plasma fractionation. XVII. Physical and chemical properties of fibrin clots, fibrin films, and fibrin plastics. *J. clin. Invest.* (In press)
6. Foerster, O., and Penfield, W. The structural basis of traumatic epilepsy and results of radical operation. *Brain*, 1930, *53:* 99–119.
7. Frantz, V. K. Absorbable cotton, paper and gauze (oxidized cellulose). *Ann. Surg.*, 1943, *118:* 116–126.
8. Grey, E. G. Fibrin as a haemostatic in cerebral surgery. *Surg. Gynec. Obstet.*, 1915, *21:* 452–454.
9. Harvey, S. C. The use of fibrin paper and forms in surgery. *Boston med. surg. J.*, 1916, *174:* 658–659.
10. Ingraham, F. D., and Alexander, E. Experimental application of sulfonamide drugs to the cerebral cortex. *New Engl. J. Med.*, 1942, *227:* 374–378.
11. Morrison, P. R., and Singer, M. Chemical, clinical and immunological studies on the products of human plasma fractionation. XVIII. Note on the absorption rates of fibrin films in tissue. *J. clin. Invest.* (In press)
12. Penfield, W. Epilepsy and surgical therapy. *Arch. Neurol. Psychiat., Chicago*, 1936, *36:* 449–484.
13. Penfield, W., and Erickson, T. C. Epilepsy and cerebral localization. *Springfield, Ill.: Charles C Thomas*, 1941, 623 pp.
14. Pudenz, R. H., and Odom, G. L. Meningocerebral adhesions. An experimental study of the effect of human amniotic membrane, amnioplastin, beef allantoic membrane, Cargile membrane, tantalum foil, and polyvinyl alcohol films. *Surgery*, 1942, *12:* 318–344.
15. Putnam, T. J. The use of thrombin on soluble cellulose in neurosurgery. *Ann. Surg.*, 1943, *118:* 127–129.
16. Seegers, W. H., and McGinty, D. A. Further purification of thrombin: probable purity of products. *J. biol. Chem.*, 1942, *146:* 511–518.
17. Unruh, C. C., and Kenyon, W. O. Investigation of the properties of cellulose oxidized by nitrogen dioxide. *J. Amer. chem. Soc.*, 1942, *64:* 127–131.
18. Yackel, E. C., and Kenyon, W. O. The oxidation of cellulose by nitrogen dioxide. *J. Amer. chem Soc.*, 1942, *64:* 121–127.

RADIOGRAPHIC CONTROL FOR PARAVERTEBRAL INJECTION OF ALCOHOL IN ANGINA PECTORIS*

CAPTAIN JAMES C. WHITE (MC) U.S.N.R. AND
ROBERT W. GENTRY, M.D.

Surgical Research Laboratories, Harvard Medical School and Neurosurgical Service, Massachusetts General Hospital, Boston, Massachusetts

(Received for publication November 23, 1943)

SINCE MANDL (1925) and Swetlow (1926) proposed paravertebral infiltration of the upper thoracic sympathetic ganglia with procaine and alcohol for the relief of intractable angina pectoris, this method has been used with increasing success. With experience it has become apparent that the results are thoroughly satisfactory if the upper three or four thoracic ganglia and their rami are thoroughly impregnated. It must be borne in mind, however, that alcohol, even when injected in 5 cc. amounts, will not diffuse far in the loose areolar tissue between the parietal pleura and the sides of the vertebral bodies. It must therefore be injected within very close proximity to the ganglia in order to be present in sufficient concentration to ensure their destruction.

Three years ago one of us (White, 1940) described an improved technique for placing needles against the sides of the upper four thoracic vertebrae for chemical blocking of the thoracic cardiac nerves,† the sympathetic ganglia, and the white rami communicantes. These structures carry afferent impulses from the heart to the corresponding spinal nerves and from there they run over posterior roots into the spinal cord. This technique has been used in the last 20 patients out of a total series of 76. The results have been satisfactory in 85 per cent of these patients, followed from one to twenty-seven months; 14 of them have had complete relief from their distressing attacks, and 3 have had their former intractable pain so reduced that it could be satisfactorily handled with routine medical methods. There were 2 failures, and 1 patient died of a painless coronary occlusion shortly after the injection. The two failures were due to inaccurate anatomical placement of the needles, especially the upper ones inserted under the first and second ribs. The exact situation of the sclerosing solution was brought out by injecting ¼ cc. of lipiodol before removing the needles and checking its position by subsequent x-ray. The radio-opaque oil showed that the injection must have missed the first thoracic ganglion, because the tip of the needle was inserted too far caudally or to an insufficient depth. From a physiological viewpoint,

* This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth are those of the writers and are not to be construed as reflecting the policies of the Navy Department.

† The cervical ganglia do not require blocking, because there are no direct connections between them and the spinal cord. All painful impulses which reach these upper ganglia over the cervical cardiac nerves must descend in the sympathetic chain at least as far as the first thoracic ganglion before they can enter the spinal nerves over the white communicant rami.

failure to destroy the first and second thoracic ganglia was evident, because the patient did not develop vasomotor and sudomotor paralysis of the side of the head and arm and a Horner's sign. While the latter is not an absolute essential, it has been our experience that satisfactory relief of cardiac pain cannot be counted on unless the hand becomes warm and dry from blocking the vasoconstrictor and sudomotor fibres which also run through these upper thoracic ganglia. The problem of effective cardiac deafferentiation by chemical block therefore resolves itself into one of more accurate insertion of the needles, especially the upper two, which are the most difficult to place. While the injection of lipiodol helped us to determine the cause of our failures, it was of no assistance in preventing them.

FIG. 1*a*. Diagrammatic view of patient in bed with needles inserted against the sides of the upper four thoracic vertebrae, to show position of x-ray tube and cassette. These injections are done on the side to which the pain is referred. In angina pectoris a left-sided injection is done for pain referred to the left arm and precordium. However, the injection must often be made bilaterally in two separate stages, and occasionally a right-sided injection is required for pure right-sided pain.

We have recently discovered that this difficulty can be overcome if a portable x-ray is taken after the needles have been inserted according to the usual technique based on the bony anatomical landmarks (White, 1940). The position of the patient for injection under radiographic control is shown diagrammatically and photographically in Fig. 1, *a* and *b*. The film taken in the oblique position shows the relation of the needles to the bodies of the vertebrae. For one who is not thoroughly accustomed to paravertebral injection, the procedure may be carried out in the x-ray department on the fluoroscopic table, so that more frequent visualization of the needles may be obtained in the course of their insertion. In general, however, we prefer to carry out these injections with the patient in his bed and to take the films with a portable apparatus. This obviates the necessity of transferring the patient from the x-ray table back to his bed, a manoeuvre which may shift the position of the alcohol and cause severe pleural pain. One or, at most, two lateral oblique films should be all that are necessary to ascertain that the tips of the needles have been placed in contact with the sides of the appropriate vertebrae and inserted to the depth of the sympathetic chain, a posi-

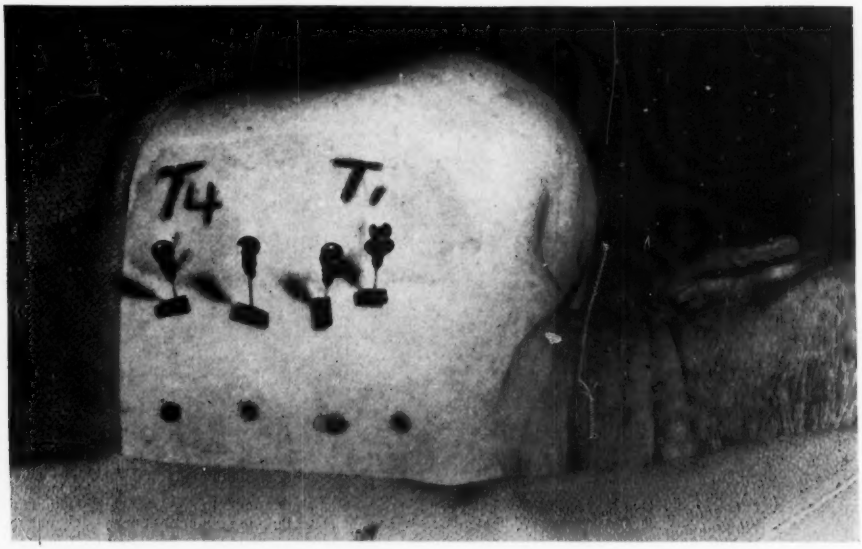


FIG. 1*b*. Photograph of patient with needles in position.

tion which ensures a chemical barrage between the ganglionated sympathetic chain and the heart anteriorly, as well as the spinal nerves posteriorly. No film from another angle is necessary, because the needle tips are always kept in contact with bone.

FIG. 2. Oblique x-ray to show position of ganglionated sympathetic chain in upper thorax in a cadaver. The position of the inferior cervical ganglion is marked by the loop in the wire and the upper two metal clips. That of the succeeding five thoracic ganglia is shown by the lower clips. Note that the first thoracic ganglion lies nearly at the anterior edge of the corresponding vertebra.

FIG. 3. Oblique x-ray to show position of needles taken during an actual paravertebral injection. This patient developed a striking Horner's sign and a hot, dry hand, as proof of the effective impregnation of the upper ganglia. The tips of the two upper needles would have been in even closer contact with the ganglia if they had been inserted a centimeter deeper.

The position of the ganglionated sympathetic chain is shown in Fig. 2. This x-ray was made from a cadaver in which the position of the sympathetic trunk was marked by a metal wire and the ganglia by dural clips. By comparing this view with Fig. 3, made in the course of an actual paravertebral injection, a good idea is given of the depth to which the needles must be in-

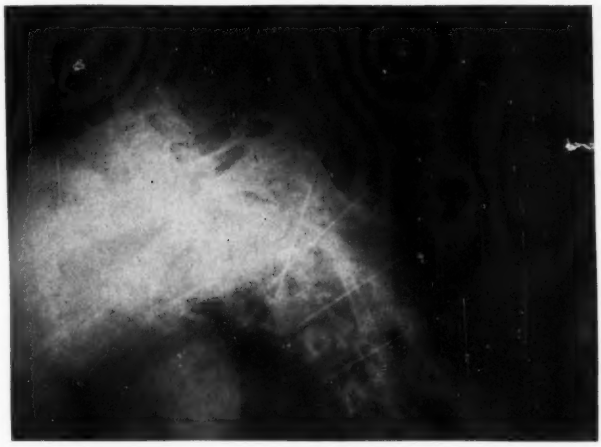


FIG. 4. Oblique x-ray taken after preliminary insertion of needles. This illustrates a common cause of failure to impregnate the first thoracic ganglion. The uppermost needle has been inserted pointing too far caudalwards, so that its tip, instead of being in contact with the side of the first thoracic vertebra, is touching the lower edge of the second.

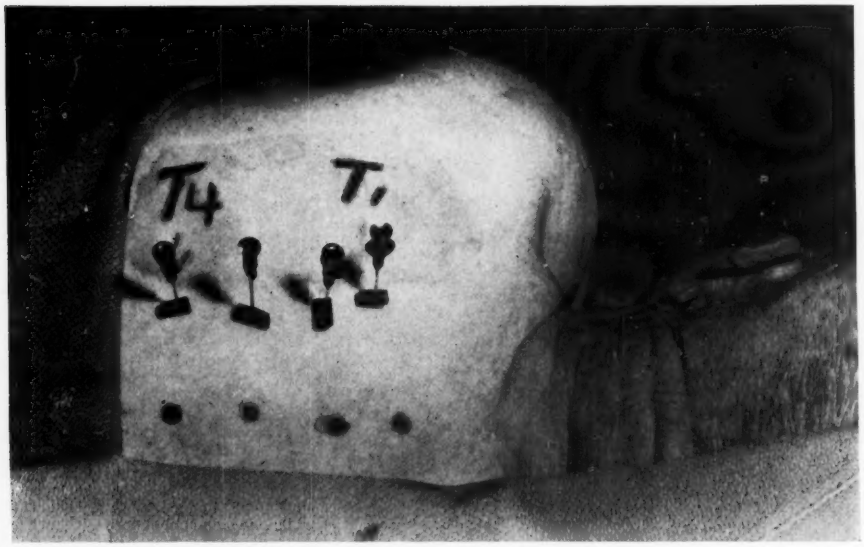


FIG. 1*b*. Photograph of patient with needles in position.

tion which ensures a chemical barrage between the ganglionated sympathetic chain and the heart anteriorly, as well as the spinal nerves posteriorly. No film from another angle is necessary, because the needle tips are always kept in contact with bone.

FIG. 2. Oblique x-ray to show position of ganglionated sympathetic chain in upper thorax in a cadaver. The position of the inferior cervical ganglion is marked by the loop in the wire and the upper two metal clips. That of the succeeding five thoracic ganglia is shown by the lower clips. Note that the first thoracic ganglion lies nearly at the anterior edge of the corresponding vertebra.

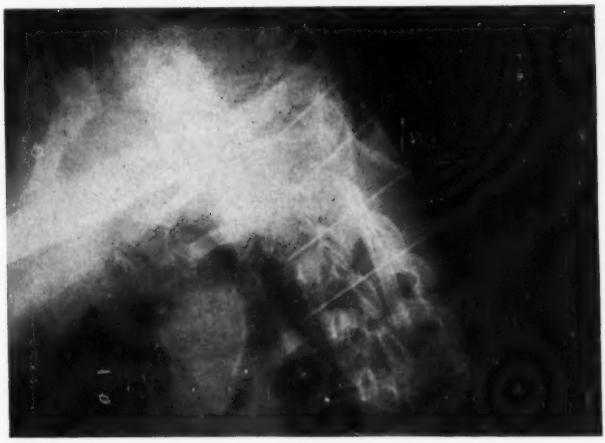


FIG. 3. Oblique x-ray to show position of needles taken during an actual paravertebral injection. This patient developed a striking Horner's sign and a hot, dry hand, as proof of the effective impregnation of the upper ganglia. The tips of the two upper needles would have been in even closer contact with the ganglia if they had been inserted a centimeter deeper.

The position of the ganglionated sympathetic chain is shown in Fig. 2. This x-ray was made from a cadaver in which the position of the sympathetic trunk was marked by a metal wire and the ganglia by dural clips. By comparing this view with Fig. 3, made in the course of an actual paravertebral injection, a good idea is given of the depth to which the needles must be in-

FIG. 4. Oblique x-ray taken after preliminary insertion of needles. This illustrates a common cause of failure to impregnate the first thoracic ganglion. The uppermost needle has been inserted pointing too far caudalwards, so that its tip, instead of being in contact with the side of the first thoracic vertebra, is touching the lower edge of the second.

serted to ensure the maximum concentration of procaine and alcohol around the upper four thoracic ganglia and their cardiac rami. The first and second thoracic ganglia lie nearly at the anterior edge of the corresponding vertebral bodies. Fig. 4 illustrates a frequent cause of failure to block the important first thoracic ganglion. Due to the moderate kyphosis of the upper thoracic spine, the operator tends to insert the upper two needles in an increasingly caudal direction and, because 7 to 8 cm. of the 10 cm. needle lies hidden beneath the skin, it is hard to realize that the tip of the first may actually be placed caudal to the second. In this case no alcohol will reach the first thoracic ganglion, and the relief of angina pectoris will often be incomplete. We believe that this accounts for the frequent failure to obtain a definite Horner's sign, and that it is of great importance to make sure that the shafts of all four needles lie parallel to one another. Such a mistake will be brought out clearly and the error prevented if the position of the needles is checked radiographically prior to injection.

In the patient in whom the position of the needles was first checked in this way, difficulty had been encountered in producing the characteristic signs of a successful blocking of the upper two thoracic ganglia with the small quantity (2 cc.) of procaine that we regularly inject as a clinical test of the accurate placement of the needles. The x-ray shows that the uppermost needle had been inserted too far caudalwards, and that its tip had completely missed the first and was touching the lower edge of the second thoracic vertebra (as shown in Fig. 4). After removal and reinsertion of this needle in a more cephalad position, it came to lie in the proper position against the body of the first thoracic vertebra (Fig. 3). This film also shows that the tips of the needles had been pushed well forward on the bodies of the vertebrae, although an additional 5 to 10 mm. would have been even more effective in laying down a chemical barrage between the ganglionated sympathetic chain and the heart. The patient developed a striking Horner's sign and remained free of precordial and arm pain. He died painlessly of coronary infarction three months later.

We believe that this simple method of checking the position of the needles by x-ray will be a distinct aid in the accuracy of paravertebral injection for the chemical destruction of the cardiac sensory axons.

We wish to express our indebtedness and sincere thanks to Dr. G. W. Holmes, Acting Chief of the X-ray Department, and to Mr. O. E. Merrill, who has taken these portable films.

REFERENCES

1. Mandl, F. Die Wirkung der paravertebralen Injektion bei "Angina pectoris." *Arch. klin. Chir.*, 1925, *136:* 495–518.
2. Swetlow, G. I. Paravertebral alcohol block in cardiac pain. *Amer. Heart J.*, 1926, *1:* 393–412.
3. White, J. C. Technique of paravertebral alcohol injection. *Surg. Gynec. Obstet.*, 1940, *71:* 334–343.

MULTIPLE MENINGIOMAS. REPORT OF TWO CASES

JOSEPH A. MUFSON, M.D., AND LEO M. DAVIDOFF, M.D.
Department of Neurosurgery, Jewish Hospital of Brooklyn, Brooklyn, New York

(Received for publication December 1, 1943)

IN CUSHING'S SERIES[3] of 2,203 verified intracranial tumors, the meningiomas comprised 13.4 per cent. The incidence has been reported as somewhat higher by others (Olivecrona,[13] 15.8 per cent; Craig,[16] 14.9 per cent; Horrax,[10] 19 per cent). Despite its frequent occurrence among brain tumors, the meningioma is rarely seen as a multiple growth unless one includes those cases of centralized neurofibromatosis, a manifestation of von Recklinghausen's disease, in which the dura is often studded with innumerable small meningiomas. Cushing and Eisenhardt[3] have preferred to designate this condition, which is usually associated with bilateral acoustic tumors, as *meningiomatosis* rather than to include it in the group of multiple meningiomas. Using this strict classification, they were able to isolate only three examples of true multiple meningiomas from their series of 295 cases of intracranial meningiomas.

The first case of multiple meningiomas reported was that of Anfimow and Blumenau[1] in 1889, who found at necropsy four large and several smaller dural endotheliomas. Similar cases have been reported by others (Krivy,[12] Flick,[5] Üprus[19]). Hosoi,[11] who reviewed the subject in 1930, was able to collect 22 cases of multiple meningiomas in the literature. Eleven of these (50 per cent) were associated with other intracranial tumors, chiefly acoustic neuromas, and consisted of a diffusion of tumor nodules over the dura. Cushing would classify these cases as "meningiomatosis." Hosoi's case, although not associated with acoustic neuromas, was accompanied by multiple angiomas in the cortex of the right frontal lobe. Frazier and Alpers[6] in their report of 75 verified meningiomas included one example of multiple tumors (Case XIV). Of 60 cases of meningioma reported by Horrax,[10] the growths were multiple in four (no mention is made of associated stigmata of von Recklinghausen's disease).

The successful removal of multiple meningiomas has been rarely reported. Heuer and Dandy[9] in 1916 reported the first successful removal of two adjacent dural endotheliomas, one having recurred after a preceding operation. Similar cases have been reported by Raaf and Craig,[16] Woltman and Love,[20] Puusepp,[15] Cushing and Eisenhardt,[3] and Echols.[4] In most instances, only two or three tumors were removed. Cushing's patient underwent five operations over a period of 14 years. One meningioma was removed at each of the second, third and fourth operations. At the fifth operation, numerous small confluent meningiomatous tumors were removed in addition to a large parasagittal growth. In Echol's case, 9 small ones and 1 large meningioma were successfully removed.

A review of the material at this clinic revealed that 58 patients with in-

tracranial meningiomas were operated upon during the past six years. Of these, four may be considered as multiple growths. Two of these fall into the group of diffuse dural meningiomatosis associated with central neurofibromatosis. One of these two, in addition to bilateral acoustic tumors, displayed at necropsy a generalized neurofibromatosis of the spinal nerve roots and cutaneous evidence of von Recklinghausen's disease. The remaining two cases, the basis of the present report, fall into the group of true multiple meningiomas as delineated by Cushing and Eisenhardt.

CASE REPORTS

Case 1 is of unusual interest not only because 10 meningiomas were removed in 4 successive operations but also because of the graphic histological transition from a benign psammomatous tumor disclosed at the original operation to an unquestionably malignant meningioma when removed at the fourth operation. In Case 2, two distinct meningiomas were successfully removed in one operation. One was a typical left frontal parasagittal tumor arising from the falx, the other a smaller growth in the left inferior frontal region which extended into the lips of the Sylvian fissure.

Case 1. E. L., a 56 year old salesman, was admitted to the Jewish Hospital on January 14, 1940. For 6 months his family had noticed a marked change in the patient's personality.

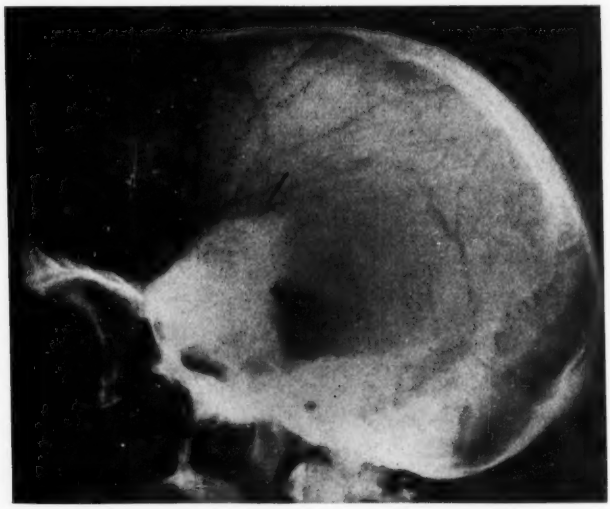


FIG. 1. Case 1. Lateral roentgenogram of skull showing dense shadow of calcified meningioma (arrows).

From an alert, aggressive type he had become a quiet, meek, apathetic individual who preferred to sit quietly by himself. Within a short time he found it difficult to concentrate and soon he became slovenly in his habits and careless about his dress. There had been no headache, vomiting or visual disturbances.

Physical Examination. The patient appeared slightly dazed but otherwise was cooperative and well oriented. There were slight disturbances of recent memory. The neurological status was essentially negative except for slight blurring of the right optic disc, complete absence of the abdominal reflexes, and generally overactive tendon reflexes.

Laboratory Data. Roentgenograms of the skull (Fig. 1) revealed a large calcified mass in the anterior portion of the right middle fossa which measured 5 ×6 centimeters in the antero-posterior projection and which appeared to originate from the lesser wing of the sphenoid bone. The mass was thought to represent a calcified meningioma.

Operation I. On January 19, 1940, under avertin and ether anesthesia a right fronto-

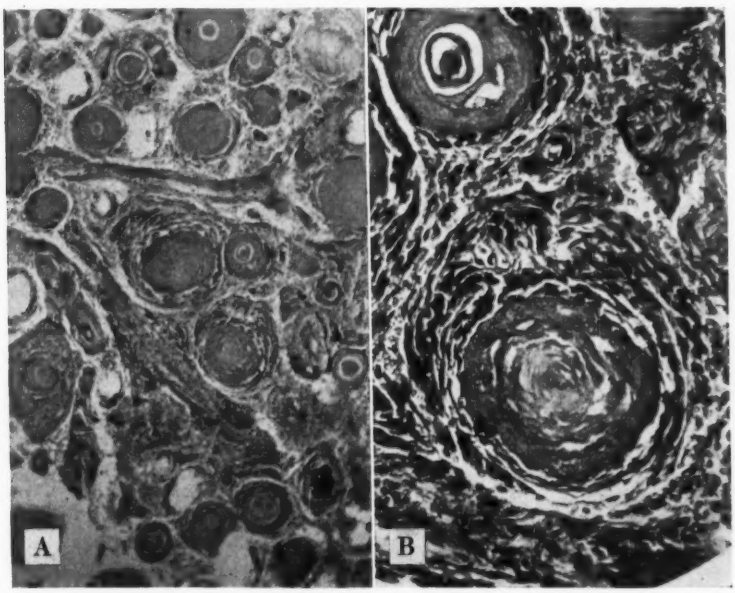


FIG. 2. *A.* Case 1. Photomicrograph of psammomatous meningioma (H.E. ×100) removed at first operation. *B.* Same ×350.

temporal craniotomy was performed. A large encapsulated tumor, arising from the lesser wing of the sphenoid, was removed piece-meal. The mass was firmly adherent to the base of the skull. After its removal, the bed of the tumor was cauterized to destroy any fragments of tumor which remained.

Histology (Fig. 2). The tumor was a typical benign meningioma. The sections showed a large number of psammoma bodies, some of which coalesced to form areas of calcification of considerable size. Fewer areas consisted of predominantly elongated cells, closely packed, and frequently describing curves with some whorl formation. There were no mitotic figures. The cells were all uniform in size and shape.

Course. The post-operative convalescence was uneventful except for a right external rectus palsy and a right peripheral facial weakness. He was discharged on the nineteenth post-operative day. Roentgenograms of the skull taken before discharge revealed complete disappearance of the pre-operative calcification.

Interval Note. Following operation the patient remained mentally sluggish and apathetic. He spent most of the time in bed. Because of slow recuperation he was referred back to the hospital for study.

Second Admission. March 26, 1940. The patient remained in the hospital for three weeks during which he was given a high caloric diet with supplementary vitamin B complex and liver. At the time of discharge, he showed marked improvement.

Interval Note. During the next two years, the patient was completely asymptomatic. He returned to work and was able to conduct his business as well as formerly. In June, 1942, however, there was a recurrence of the same personality deficits noted prior to his first admission. He began to complain of pain about the right eye and cheek and noticed that his left arm was weaker than formerly.

Third Admission. July 9, 1942. Examination at this time revealed the patient to be quite

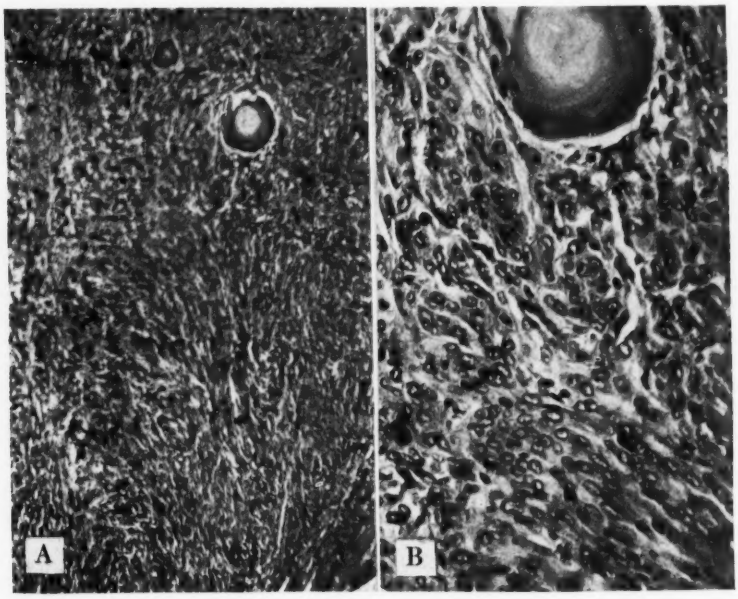


FIG. 3. *A.* Case 1. Photomicrograph of cellular fibroblastic meningioma with occasional psammoma body removed at second operation (H.E. ×100). *B.* Same ×350.

dull mentally. He was slightly disoriented and showed disturbance of recent memory. There was a left homonymous hemianopsia. The optic discs were pale. There was a left hemiparesis, an exaggerated left knee jerk, a left Hoffman sign but no Babinski. Position sense, vibratory perception, 2-point discrimination were all impaired in the left upper limb. There was astereognosis on the left.

A pneumoencephalogram was made on July 15, 1942. This revealed a failure of the right ventricle to fill with gas. The left ventricle, however, was enlarged and was definitely displaced to the left. In some views the third ventricle was visualized and also appeared displaced to the left.

Operation II. On July 17, 1942, the previous bone flap was re-elevated. A spherical, encapsulated tumor mass about 3 cm. in diameter was found in the anterior portion of the middle fossa in the region of the outer third of the sphenoid wing. The tumor was attached to the lateral dura and not to the base of the skull as in the previous operation. Nevertheless the tumor was thought to represent a recurrence of the original growth.

Histology (Fig. 3). The tissue was quite cellular consisting of sheets of cells with poorly defined cell borders. There was some tendency to whorl formation and an occasional psammoma body was seen. The cells in some areas showed slight variation in size and shape. There was slight tendency toward nuclear clumping but true multinucleated cells were not visible. No mitotic figures were seen. Laidlaw's connective-tissue stain revealed an extensive reticulin and collagen network throughout the tumor. In many areas the cells were spindle-shaped and clearly of fibroblastic type.

Course. The immediate post-operative reaction was satisfactory. The patient, however, continued to exhibit marked disturbance of sensorium. He developed bowel and bladder in-

FIG. 4. Case 1. Three meningiomas removed at third operation.

continence. Gradually these symptoms improved. He was allowed out of bed on the twelfth post-operative day and discharged on the twenty-first post-operative day. At the time of discharge, the incontinence had disappeared and the patient was oriented and alert.

Interval Note. The patient continued to improve at home but within two months, he again presented himself for admission because of severe headache and increasing weakness of the left upper and lower limbs.

Fourth Admission. October 11, 1942. Examination at this time again revealed slight disturbances of orientation and memory. The left hemiparesis had increased slightly. It was difficult to conceive of another recurrence in so short an interval. Nevertheless another pneumoencephalogram was made. This revealed a tremendous shift of the ventricular system to the left. Operation was advised but the family did not consent and the patient was discharged to a nursing home on November 18, 1942.

Interval Note. He continued to go downhill. The mental symptoms and the hemiparesis increased. Because of the rapid progression, he was brought back for operative intervention.

Fifth Admission. December 30, 1942. Examination was similar to that of the previous admission except for the increase in the mental deficit and progression of the hemiparesis.

Operation III. On January 4, 1943, the previous bone flap was re-elevated. Anteriorly where the previous tumor had existed, there was a large empty space filled with clear fluid.

In the posterior inferior half of the exposure, there was a rather large encapsulated tumor adherent to the tentorium in the region of the lateral sinus. It measured approximately 5 cm. in diameter. It was necessary to extend the cranial defect posteriorly to attack this mass. The tumor was removed completely and its bed coagulated. With this out of the way, there came into view another tumor in approximately the same region of the tentorium but more medially placed. It was smaller than the first, measuring about 3 cm. in diameter. This tumor was removed in a manner similar to the first. With this accomplished, a third tumor came into view even more medially placed than the second. This too was excised and after careful inspection revealed no further tumor masses, the procedure was terminated (Fig. 4).

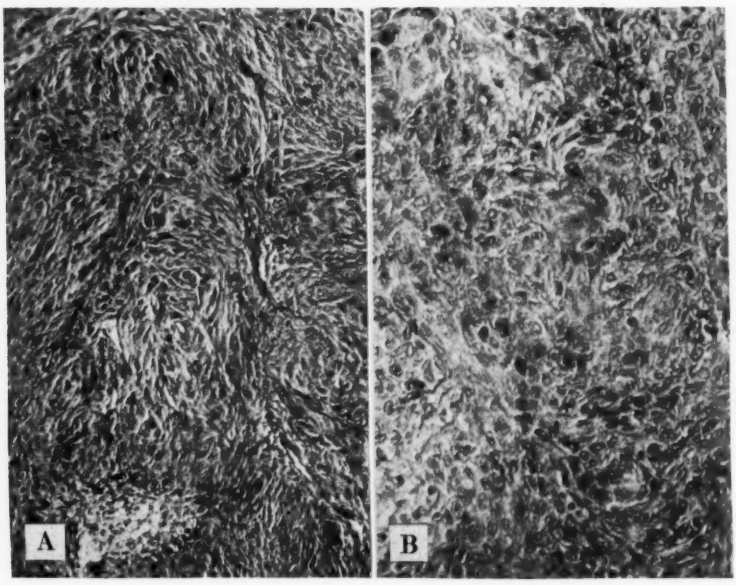


FIG. 5. *A*. Case 1. Photomicrograph of meningiomas removed at third operation (H.E. ×100). Appearance essentially similar to Fig. 3 except that cells are slightly more variable, areas of necrosis are present; occasional mitotic figures; disappearance of psammoma bodies. *B*. Same ×350.

Histology (Fig. 5). Sections taken from different portions of the 3 tumors showed essentially the same microscopic appearance. The tissue was fairly cellular, the cells being irregularly round, oval, or elongated and of medium size. In some areas they showed a moderate degree of variation in size and shape. An occasional mitotic figure was seen. Some areas showed definite whorl formation. There were focal areas of necrosis scattered throughout the tumors and these areas contained numerous fat-filled cells and granular debris. In some areas finger-like projections of tumor were present in the adherent brain. The tumor was permeated by a rich reticulin and collagen stroma. The tumors resembled those previously removed although there was more variation in the cell type on this occasion.

Course. Post-operative convalescence was slow. The patient ran an unexplained spiking temperature for three weeks during which his mental status became even more deteriorated. At this point the temperature gradually returned to normal and coincidentally his sensorium cleared. The hemiparesis began to improve. He was discharged on the fifty-first post-operative day.

FIG. 6. Case 1. Five meningiomas removed at fourth operation.

Interval Note. The improvement was short-lived. Five weeks after discharge, the patient developed persistent hiccough and progressive jaundice. He was referred for admission to the medical service.

Sixth Admission. March 27, 1943. Examination revealed in addition to generalized jaundice, a large tender liver, a palpable spleen and a temperature of 101°F. Four days after admission he had a massive hematemesis. The hemoglobin fell to 44 per cent. He was treated with repeated transfusions. The jaundice and fever gradually receded and he was discharged to a nursing home on April 13, 1943. The episode of jaundice was interpreted as due to acute hepatitis.

Interval Note. The patient continued to improve during the months of April, May and June. He became mentally alert and, according to the family, was again his "former self." He soon began to walk with the aid of a cane. Again our optimism was to no avail for in July, six months following the third operation, there were again symptoms of recurrence. His sensorium became cloudy and he began to complain of severe headaches over the right half of the head. He became increasingly drowsy and soon sphincteric incontinence appeared.

Seventh Admission. October 20, 1943. A pneumoencephalogram was made on October 22, 1943, and revealed once more a shift of the lateral and third ventricles to the left. In addition gas in the fourth ventricle appeared displaced to the left. In view of our previous experience, there was every indication that we were dealing with one and probably multiple recurrent tumors.

Operation IV. November 1, 1943. Upon re-elevating the original bone flap once more a

large empty space filled with clear fluid could be seen through a defect in the dura. This space represented the site of removal of the previous tumors. The dural defect was enlarged and four small meningiomas came into view. One was over the convexity of the brain, two were attached to the sphenoid wing, and a fourth occupied the base of the skull in the anterior part of the middle fossa. This last tumor eventually proved to be a large growth extending through the base of the skull. Further search revealed a fifth and even larger tumor attached to the tentorium in the region of the petrous bone. This mass was found to extend medially through

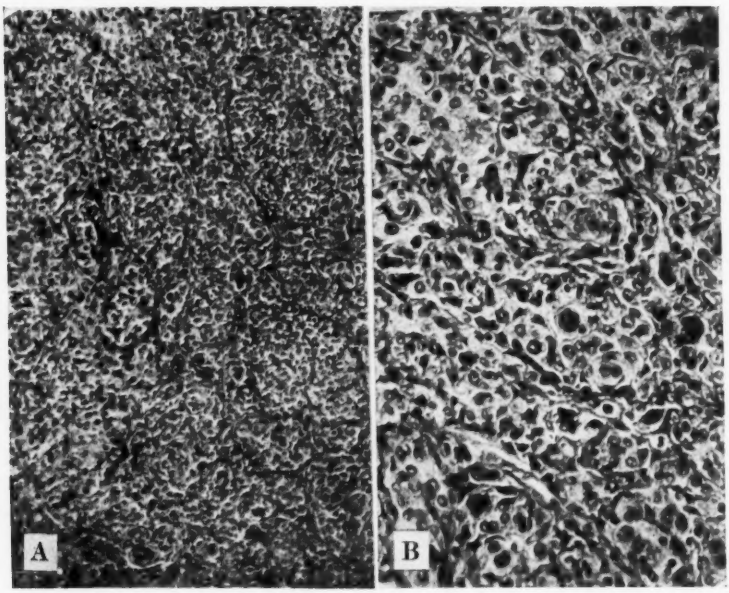


FIG. 7. *A*. Case 1. Photomicrograph of one of the tumors removed at fourth operation. Note the considerable variability in size and shape of cells, the nuclear clumps, giant cells, mitotic figures (H.E. ×100). *B*. Same ×350.

the tentorium into the posterior fossa (Fig. 6). Chronologically this tumor was removed first separating it from the surface of the cerebellum and pons. Then the three superficial tumors were removed. Finally the fourth, extending through the base of the skull, was attacked. This could not be removed cleanly but what shaggy remains were seen were thoroughly coagulated.

Histology (Fig. 7). Sections taken from different portions of the various tumors showed a variable microscopic appearance. In some sections there were numerous whorls and some psammoma bodies. In most of the sections there were moderate numbers of mitotic figures. In sections taken from two of the tumors, there was considerable variation in the size and shape of the cells, which presented no definite architectural pattern. The cells were, for the most part, of medium size with round or oval nuclei and usually without nucleoli. The cytoplasm was rather ill-defined and there was some tendency toward nuclear clumping. Blood vessels were moderate in number and their walls were well formed.

These sections differed strikingly from those of the previous tumors. The first specimen showed a predominance of psammoma bodies and whorls. This tendency gradually became less marked. There was no doubt, in reviewing the various sections of all the tumors, that

there had been a progressive tendency toward a malignant change with some of the last tumors being obviously malignant.

Course. The immediate post-operative reaction was satisfactory. However, the patient failed to regain consciousness. His breathing became rapid and stertorous, he sank deeper into coma, and despite supportive measures, expired forty-eight hours following operation.

Necropsy. The dura over the right frontal parasagittal region contained several pea-sized

FIG. 8. Case 1. Post-mortem specimen of dura showing numerous tumor nodules. Separate specimen is of neoplastic tissue between the leaves of the tentorium.

nodules (Fig. 8). In addition a flat tumor mass was present between the leaves of the tentorium cerebelli on the right side. No tumors were found on the left side of the brain and none were present in the posterior fossa. There was no evidence of von Recklinghausen's disease.

The second case was much less dramatic, but since two separate and distinct tumors were found at operation, we believe it should be included as another example of multiple meningioma in the absence of von Recklinghausen's disease.

Case 2. B. G., a 45 year old insurance broker, was admitted to the neurosurgical service of the Jewish Hospital on June 2, 1942. Eight years previously he had noticed a lump in the left temple which was accompanied by periodic sticking pains in that region. He was seen by

a general surgeon at that time, and following numerous roentgenograms of the skull and other bones of the body, a biopsy of the lump was taken. Apparently a definite histological diagnosis could not be made. The final opinion, however, was *fibrosarcoma*. Because of this, thirty x-ray treatments had been given over the region of the tumor. Four years prior to admission, within a period of two weeks, the patient had two spells of unconsciousness of short duration. Neither was witnessed. In October, 1941, he developed progressive weakness of the right lower limb, affecting chiefly the foot. Two weeks before admission he noticed a hard lump over the vertex of the skull to the left of the midline. This had not been present before.

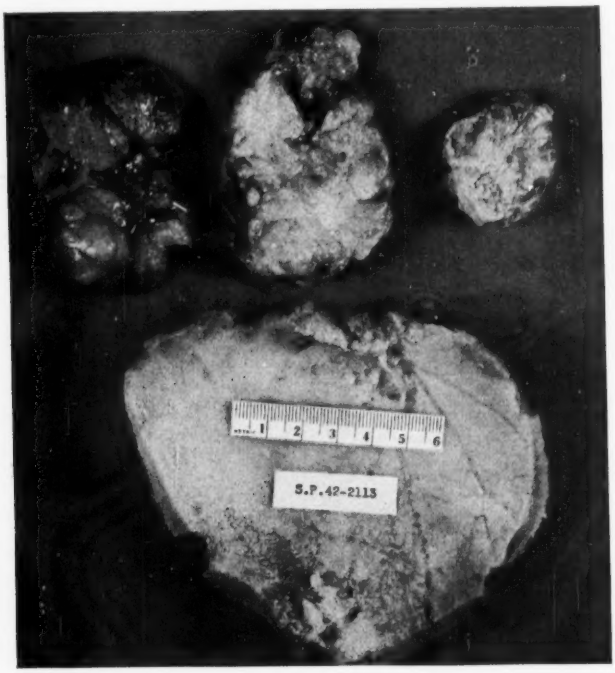


FIG. 9. Case 2, showing two halves of the larger tumor and half of the smaller one. Also the bone flap where involvement by the parasagittal tumor is seen in the inferior portion of the photograph and the Sylvian tumor in the superior portion of the photograph of the flap.

Physical Examination. The skin over the left fronto-temporal area was scarred and atrophic due to the extensive radiotherapy. Beneath the atrophic skin an irregular hyperostosis was palpable. There was, in addition, a hard bony lump in the left parasagittal region above the scar. The general examination was otherwise normal. The neurological survey revealed moderate weakness of the right lower limb, most marked in the dorsi-flexors of the foot, hyperactive right knee and ankle jerks, and a positive right Babinski sign.

Laboratory Data. Roentgenograms of the skull revealed a large area of decalcification in the left fronto-temporal region. In addition there was an area of hyperostosis in the outer table near the vertex just behind the coronal suture. This corresponded to the bony lump felt on examination of the head.

Operation. On June 9, 1942, a left fronto-temporo-parietal craniotomy was performed.

When the bone flap was turned, tumor was seen extruding through the dura and into the bone both along the parasagittal region and in the region of the pterion. The bone flap was so extensively involved with tumor that it was thought unwise to replace it and it was, therefore, removed early in the operation. Additional bone which was also involved by tumor was rongeured away. A small tumor, measuring $4 \times 1.5 \times .5$ cm., was encountered in the frontotemporal region involving the dura and extending into the lips of the Sylvian fissure. This was excised completely. The dura was then opened superiorly toward the parasagittal region. Here a second and larger tumor, measuring $7 \times 5 \times 4$ cm. and weighing 72 grams, was discovered. This was found to be adherent to the superior longitudinal sinus for a considerable distance. The tumor was removed without undue difficulty (Fig. 9).

Course. The patient's post-operative convalescence was very satisfactory. There was a transient mild aphasia and a right hemiparesis, both of which cleared rapidly. At the time of discharge on the fifteenth post-operative day, the patient was completely asymptomatic except for slight hesitancy in speech. It is now 18 months since operation. The patient is back at work and in excellent health.

Histology. The tumors were clearly meningiomas whose microscopic appearance varied considerably in different regions. In some areas the appearance was that of a psammomatous type of meningioma with whorls predominating. In other areas the fibroblastic elements were conspicuous and in still other places, the appearance was suggestive of a hemangioblastoma. There was no evidence of malignancy in any of the sections. The tumors were classified as meningiomas of mixed type.

COMMENT

Multiple meningeal tumors, as previously stated, occur either alone or in combination with centralized neurofibromatosis. Usually no attempt has been made to segregate the two types. In the von Recklinghausen type, the growths usually consist of a diffusion of meningeal tumefactions, small in size, and scattered over a wide area of the meninges. The familial nature of multiple neurofibromatosis has long been recognized (Harbitz,[8] Preiser and Davenport,[14] and Schaltenbrand[17]). More recently Gardner and Frazier[7] have shown that bilateral acoustic tumors, a special form of centralized neurofibromatosis, is also a familial and hereditary disease.

Usually no such diffusion of tumors and no such familial or hereditary relationship has been shown to exist in those cases of multiple meningiomas without the stigmata of von Recklinghausen's disease. For this reason, it seems best in the present state of our knowledge to consider them, as Cushing has done, in a separate category. The cases reported here belong to this group.

In Case 1, ten meningiomas were removed from the right hemicranium over a period of three years. The patient was under constant clinical observation throughout his illness and neither during life nor at necropsy could any of the stigmata of von Recklinghausen's disease be found.

Cushing[3] stated that the meningiomas "rarely, if ever, change their histological type and that a given tumor of sarcomatous type has been sarcomatous from the outset." He cites three of his cases in which there was no appreciable change after 12, 13 and 17 years respectively, despite frequent recurrences. In the successive tumors removed in our Case 1, however, there can be no doubt that there was a transition in histological form. During the three year period, there was a remarkable transition from a benign psam-

momatous meningioma removed at the first operation to an unquestionably malignant tumor at the fourth operation. Sections taken from the original tumor were unmistakedly those of a psammomatous meningioma, considered to be perhaps the most benign of the meningeal tumors. At the second operation, the tumor had become more cellular, there had been a marked decrease in whorl formation, and only an occasional psammoma body was seen. The picture undoubtedly represented more rapid growth. At the third operation, the general appearance of the tissue was similar to that of the previous tumor but for the first time, one began to see some variation in the size and shape of the cells and an occasional mitotic figure. There were also small areas of focal necrosis in various portions of the tumors. At the fourth operation, two of the tumors were obviously malignant, showing marked variation in the size and shape of cells, unusually large forms, giant cells, and numerous mitotic figures. The general impression was one of increasingly rapid growth in each successive tumor.

Turner, Craig and Kernohan[18] have recently studied the pathology of malignant meningomas. In their review of 370 meningeal intracranial tumors seen at the Mayo Clinic they found 36 (approximately 10 per cent) malignant growths. Applying their histological criteria, the tumors removed at the third operation in Case 1 would be considered of low grade malignancy while two of those removed at the final operation would be of pronounced malignancy. These authors cited no examples of benign meningiomas becoming malignant at subsequent operations for recurrence. That this transition occurs in certain of the gliomas has long been known. Bailey[2] has shown that a typical protoplasmic astrocytoma removed at a primary operation was transformed into a glioblastoma multiforme at a secondary operation a few years later. The changes in our case may be considered analogous to the dedifferentiation of the astrocytoma. To our knowledge there has been no similar case reported in the literature. Perhaps a more careful study of recurrent meningiomas will lead to similar cases showing different degrees of anaplasia from one operation to the next.

In reviewing the progression of events in this case, one is struck by the limitation of the meningeal growths to the right hemicranium. Both during life and at necropsy there was no evidence of involvement of the left side of the brain. The thought occurred that the multiplicity of the recurrent tumors in our case was due to spreading by implantation at the time of operation. However, Cushing[3] was aware of this hemicranial distribution of the tumors in most of the cases of true multiple meningiomas reported in the literature but he offered no explanation for it. It is to be contrasted with the meningeal tumefactions seen in cases of centralized neurofibromatosis where the distribution is practically always bilateral. Because of this and the absence of a familial or hereditary transmission in these cases, it would appear that multiple meningeal tumors are not necessarily an expression of von Recklinghausen's disease, where the defect is said to be a congenital abnormality of the ectoderm, commonly familial and often inherited as a Mendelian dominant.

In Case 2 two separate and distinct meningiomas were removed at one operation. The case is recorded merely as another instance of successful removal of multiple meningiomas. Here, as in Case 1, the tumors were limited to one side of the brain and there was no clinical evidence of von Recklinghausen's disease.

SUMMARY AND CONCLUSIONS

Two cases are presented, the one with ten meningiomas confined to the right hemicranium, removed at four operations; the other with two meningiomas removed from the left side of the brain.

In the first case the original tumor was a benign psammomatous lesion. With each episode leading to reoperation, the tumors showed a progressive tendency to more rapid growth, until one of the last tumors was definitely sarcomatous. This change appeared analogous to dedifferentiation in gliomatous tumors from more benign to more malignant types.

The absence of neurofibromatosis in these two cases leads us to classify them as cases of multiple meningioma as distinct from meningiomatosis seen accompanying von Recklinghausen's disease.

REFERENCES

1. Anfimow, J., and Blumenau, L. Ein Fall multipler Geschwülste in der Schädelhöhle. Abstracted in: *Neurol. Zbl.*, 1889, *8:* 585.
2. Bailey, P., Sosman, M. C., and Van Dessel, A. Roentgen therapy of gliomas of the brain. *Amer. J. Roentgenol.*, 1928, *19:* 203–264.
3. Cushing, H., and Eisenhardt, L. Meningiomas. Their classification, regional behaviour, life history, and surgical end results. *Springfield, Ill.: Charles C Thomas*, 1938, 785 pp.
4. Echols, D. H. Multiple meningioma. Removal of ten intracranial tumors from a patient. *Arch. Neurol. Psychiat., Chicago*, 1941, *46:* 440–443.
5. Flick, K. Fehldiagnose bei multiplen Endotheliomen der Dura. *Zbl. Chir.*, 1928, *55:* 2321–2323.
6. Frazier, C. H., and Alpers, B. J. Meningeal fibroblastomas of the cerebrum. *Arch. Neurol. Psychiat., Chicago*, 1933, *29:* 935–989.
7. Gardner, W. J., and Frazier, C. H. Bilateral acoustic neurofibromas. A clinical study and field survey of a family of five generations with bilateral deafness in thirty-eight members. *Arch. Neurol. Psychiat., Chicago*, 1930, *23:* 266–302.
8. Harbitz, F. Multiple neurofibromatosis (von Recklinghausen's disease). *Arch. intern. Med.*, 1909, *3:* 32–65.
9. Heuer, G. J., and Dandy, W. A report of seventy cases of brain tumor. *Johns Hopk. Hosp. Bull.*, 1916, *27:* 224–237.
10. Horrax, G. Meningiomas of the brain. *Arch. Neurol. Psychiat., Chicago*, 1939, *41:* 140–157.
11. Hosoi, K. Meningiomas. With special reference to the multiple intracranial type. *Amer. J. Path.*, 1930, *6:* 245–260.
12. Krivy, M. Etude anatomique d'un cas de tumeurs multiples des méninges. *Rev. neurol.*, 1926, *45:* 154–163.
13. Olivecrona, H. Cited by Wilson, S. A. K., and Bruce, A. N. Neurology. *Baltimore: Williams and Wilkins Co.*, 1940, 2 vols.
14. Preiser, S. A., and Davenport, C. B. Multiple neurofibromatosis (von Recklinghausen's disease) and its inheritance: with description of a case. *Amer. J. med. Sci.*, 1918, *156:* 507–540.
15. Puusepp, L. Cited by Echols, D. H.[4]
16. Raaf, J. E., and Craig, W. M. Multiple meningiomas: report of a case in which three intracranial meningiomas were successfully removed. *Arch. Surg., Chicago*, 1935, *31:* 601–606.
17. Schaltenbrand, G. Sobre una familia con enfermedad de Recklinghausen. *Prensa méd. argent.*, 1933, *20:* 1011–1026.
18. Turner, O. A., Craig, W. M., and Kernohan, J. W. Malignant meningiomas. A clinical and pathologic study. *Surgery*, 1942, *11:* 81–100.
19. Úprus, V. Meningioma multiplex cerebri. Abstracted in: *Zbl. ges. Neurol. Psychiat.*, 1933, *67:* 444.
20. Woltman, H. W., and Love, J. G. Multiple intracranial meningiomas with extension to the external auditory canal: successful removal: presentation of case. *Proc. Mayo Clin.*, 1935, *10:* 497–501.

A PERFORATOR AND BALL BURR

KENNETH G. McKENZIE, M.D.
Neurosurgical Division, Department of Surgery, University of Toronto, Toronto, Ontario

(Received for publication December 6, 1943)

HAND BURRS and perforators can be good, bad or indifferent. For years only the indifferent and bad appeared on my instrument table. Other surgeons may have had similar exasperating experiences. The author believes that these drills may help to clear the blue haze from those operating rooms where cutting instruments fail to cut.

Drill *A* has been in use for some years. It was originally modified from a stock metal

A Perforator. *B* Ball burr. (Actual size)

worker's drill in the hope that it would cut a hole big enough for all purposes. In the larger sizes it would not cut with satisfaction. As designed now the opening made is big enough for most ventriculographies. The taper on the drill causes it to lock and prevents plunging when the inner table is perforated.

Drill *B* is a modified ball burr which cuts with speed and with as much ease through the inner as the outer table. It is used to enlarge the opening made by *A* when a bone flap is being fashioned. It is also useful in starting the exposure for a disc as it bites well into the adjacent laminae. An extension of the ordinary Hudson drill handle is useful when the burr is used for this purpose.

The chief features of these drills are as follows:

1. They are hand fashioned from hard tool steel—that is, steel that is used to cut steel—hence the cutting edge remains sharp for months when used to cut bone. My present burrs have been in constant use for six months and still cut as well as ever.

2. The drills must be kept well oiled or they will rust and the cutting edge deteriorate. Plating prevents rust but dulls the cutting edge that these drills have, hence they are not plated.

3. The cutting edges are hand fashioned by an expert. If and when they get dull one would urge their return to the original maker for reconditioning. With care and the prevention of rust, reconditioning should be necessary at long intervals only.

4. The drills fit the standard Hudson drill handle.

5. Every alternate cutting edge on the ball burr is at a lower level, and so shaped that bone dust does not clog between the cutting edges. The burr does not chatter.

6. The ball drill bites into bone and cuts as freely through the inner as the outer table. It must of course be preceded by the perforator A.

7. The drills are sterilized by soaking in 85 per cent alcohol for one-half hour. At all times except when in actual use, the cutting edges are protected by a cloth bag which fits over the drill.

I am very grateful to Mr. H. Smart of the Illinois Tool Company, Toronto, for the interest and persistence with which he has turned out numerous ball burrs* until a model was obtained that remains extremely efficient. Lieut. Col. Spurling, Walter Reed Hospital, Washington, has been using a set of these drills for some months and seconds my satisfying experience with them.

* Manufactured by the Illinois Tool Co., Toronto, Ontario, and retailed by Down Bros., 143 College Street, Toronto, Ontario.

CEREBROSPINAL RHINORRHEA—SURGICAL REPAIR*

WILLIAM J. GERMAN, M.D.

Department of Surgery, Yale University School of Medicine, New Haven, Connecticut

(Received for publication December 16, 1943)

CEREBROSPINAL RHINORRHEA is a relatively common complication of craniocerebral injuries in the frontal region, especially when the site of impact is near the glabella.† Spontaneous arrest of the rhinorrhea may be expected within ten days in a large percentage of patients, and Adson[1] has noted spontaneous recovery as long as eight weeks after the injury. The problems and methods of surgical treatment of acute cerebrospinal rhinorrhea have been discussed by Dandy,[4] Teachenor,[11] Munro,[9] Cairns[2] and Coleman.[3] Cairns'[2] report leaves no doubt concerning the serious potentialities of chronic leak of cerebrospinal fluid into the nose. A series of twenty-one cases from the literature was reviewed by Johnston;[8] injury was an etiologic factor in six instances. The rhinorrhea persisted in nine cases and the patients were alive at the time of report; the flow had ceased in six cases. Six of the patients were dead when the reports were published.

Chronic cerebrospinal rhinorrhea may appear after an interval of several weeks following the injury. Gissane and Rank[6] designated this type as "delayed post-traumatic cerebrospinal rhinorrhea." Such a delayed onset was noted in each of the four traumatic examples in the present report. Two of these patients had recovered from pneumococcus meningitis, under intensive chemotherapy; the rhinorrhea was apparently unaltered by the meningeal infection. One instance of rhinorrhea from a nasal encephalocele is included in the present report, the nasal leak appearing after a considerable interval following intranasal "snare" excision of a "tumor." Intracranial pneumatocele was noted in one of the traumatic cases.

At present there is unanimity of opinion concerning the advisability of surgical repair of chronic cerebrospinal rhinorrhea. The methods of repair have varied considerably: Insertion of an iodoform gauze wick beneath the dural defect has been advised by Peet;[10] direct suture of the dural defect or fascia lata graft has been used by Cairns;[2] plugging the bone defect with bone wax was suggested by Graham;[7] interposition of a free periosteal graft from the tibia, between the bone defect and the dura, was successful in Gissane and Rank's case.[6] Adson[1] described a method of direct dural suture, involving bifrontal exposure, ligation of the longitudinal sinus, elevation of the dura from the floor of both anterior fossae, interposition of a muscle graft in the suture line and plugging the bone defect with bone wax which is covered with Luken's animal membrane. This procedure was used successfully in eight cases. The methods so far described depended upon extradural

* Reported in part at the meeting of the Harvey Cushing Society, May 30, 1941, Rochester, N. Y.

† Cairns[2] states this type of injury is not infrequent in aeroplane accidents.

exposure of the dural defect. Eden[5] described successful closure of cerebrospinal fistulae in two cases by fascia lata graft, applied by intradural operation.

The site of the fistula is of considerable importance in the selection of the most appropriate method of surgical repair. Anterior fistulae into the frontal sinuses can be readily exposed by the extradural approach and repaired by direct suture or suitable grafts. However, defects at the cribriform plate appear to be at least as frequent as those in the frontal sinuses; all five patients in the present report had fistulae through the cribriform plate. The extradural approach to fistulae through the cribriform plate is much more difficult because of the thin dura with its firm attachments to the bone and the tendency for these fistulae to be located more posteriorly. Extradural repair of such defects is subject to the further handicaps of the small working-space available at the side of the crista galli and the limitation of direct visualization of the dural defect by the overhanging frontal lobe. These handicaps apparently may be overcome, to a large extent, by Adson's procedure.[1] The chief reason for avoiding an intradural repair has been the potential source of meningeal infection at the fistulous site. At present, the availability of adequate chemotherapy materially reduces this hazard.

The purpose of the present report is to present a simple method of intradural repair of cerebrospinal rhinorrhea which has been used successfully for the past five years. The method of Adson[1] was not available when the first case in this series was treated in 1938. It appeared that the ideal form of repair should be one in which a dural flap could be utilized to cover the defect in the cribriform plate; the dura covering the crista galli suggested itself as the logical source for this flap. Repair was readily effected in this manner, even in the limited space available in a child of eleven months.

DURAL-FLAP METHOD OF REPAIR

A frontal osteoplastic bone flap is elevated on the side corresponding to the nasal leak and the dura opened along the anterior margin of the exposure. The frontal lobe is gently retracted until the floor of the anterior fossa can be seen. The site of the fistula may be identified by the attachment of the adjacent cerebrum to the dural defect. This attachment was composed of meningocortical scar in the four traumatic cases in this series. The scarred cerebral parenchyma may be herniated through the defect; this is probably an important mechanism, preventing spontaneous closure. The attachment is divided with an electro-surgical unit and the meningocortical scar may be excised if desired. A dural flap (Fig. 1) is then constructed from the dura covering the crista galli and this flap may be continued to include the anterior portion of the falx, if considerable dura is required. The flap is hinged at the base of the crista galli, folded across the defect in the cribriform plate and sutured to the dura at the lateral aspect of the defect, using small curved needles and fine silk. In two cases it was necessary to use a supplementary procedure, due to an extensive dural defect lateral to the fistula. In one in-

stance, a lateral dural flap was constructed from the dura covering the lateral portion of the floor of the anterior fossa; this flap was folded medially and sutured to the margins of the medial flap. In the other case, a free periosteal graft from the bone flap was used to cover the large lateral defect; the graft was sutured to the dural margins and to the medial flap. Topical application of sterile sulfonamide powder may be used in the bone defect. Bone wax has

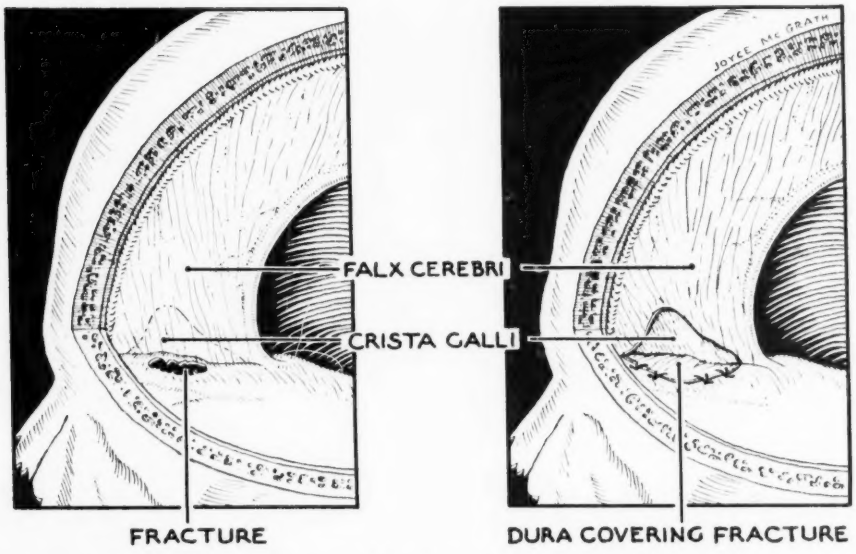


FIG. 1. Diagrammatic illustration of a defect in the cribriform plate and its repair by a dural flap from the crista galli. The flap may be extended upward to include a portion of the falx, if a larger flap is required.

not been used because of potential contamination at the fistulous site. Since the dural flap from the crista galli and falx tends to span the olfactory groove, a small muscle graft is tucked under the posterior edge of the dural flap, filling this portion of the olfactory groove. The olfactory nerve is usually found to have been severely damaged at the initial injury, but in one case it was possible to preserve the olfactory nerve.

This procedure has been used successfully in five cases. Sulfonamide medication is given for an appropriate period before and after operation.

CASE REPORTS

Case 1. (N.H.H. #A78145). A girl of eleven months, whose left nostril was noted to have been obstructed, shortly after birth, had a nasal "tumor" excised with a snare at the age of seven months. The pathological diagnosis of the excised tissue was encephalocele. During the succeeding three months the nasal encephalocele gradually increased in size. Cerebrospinal rhinorrhea appeared one week before admission to the hosiptal, July 12, 1938. Sulfonilamide was started shortly after rhinorrhea began.

Examination revealed a slightly retarded child of eleven months, who was unable to sit without support. The left nostril was obstructed by a gray mass from which clear fluid leaked, with changes of head position; the fluid contained 10 lymphocytes per c.mm.; nose culture: staphylococcus. X-rays of the skull were normal; there was no demonstrable air within the cranium. Laboratory findings were normal except for leucocytosis of 19,500.

Operation: A left frontal osteoplastic bone flap was elevated and the dura was opened. The frontal lobe was elevated and the stalk of the meningocele was identified as it passed through a defect, 8×3 mm., in the left olfactory groove, posterior to the olfactory bulb. The stalk was fulgurated and a flap from the dura covering the crista galli was sutured over the defect in the olfactory groove. There was no recurrence of cerebrospinal rhinorrhea and the nasal mass gradually decreased in size. Convalescence was complicated by local infection of the edge of the bone flap.

Case 2. (N.H.H. #A91643). A woman of 26 years was struck on the right side of the forehead by a stone which fell from a truck while passing the automobile in which she was riding. She was unconscious four days and later noted intermittent dripping of clear fluid from the right nostril. On one occasion the rhinorrhea was absent for three years but then returned spontaneously. Nine and one-half years after the injury, an upper respiratory infection was followed by pneumococcus type VI meningitis. She was treated with sulfapyridine and anti-pneumococcus (rabbit) serum, type VI. Convalescence was uneventful but the rhinorrhea continued. Six months later she entered the hospital for surgical repair of cerebrospinal rhinorrhea.

Examination revealed a normal appearing woman of 36 years. There was complete anosmia, slight pallor and blurring of the margins of the optic discs; the right pupil was a trifle larger than the left. Rhinorrhea was absent at the time of the examination. X-rays of the skull failed to demonstrate abnormalities other than hyperostosis frontalis interna and calcification of the falx. Sulfapyridine was given for two days, resulting in a preoperative blood level of 11.2 mgm. per cent.

Operation: A right frontal bone flap was elevated and the dura was opened along the anterior margin of the exposure. The frontal lobe was elevated, exposing a meningocortical scar attaching the inferior portion of the frontal lobe to a deep fissure, 25×8 mm., in the cribriform plate. The scar was freed and a flap of dura from the crista galli and adjacent falx was sutured over the defect. Small muscle grafts were inserted beneath the anterior and posterior edges of the dural flap, to fill the olfactory groove. The right olfactory nerve had been completely destroyed by the original trauma. Sulfapyridine medication was continued for five days after operation. Convalescence was uneventful except for the late appearance of sterile fluid at the site of the anterior-medial burr hole of the bone flap. Cerebrospinal rhinorrhea has not recurred.

Case 3. (N.H.H. #B11169). A 30 year old motorcycle policeman was injured in a head-on collision with a truck, October 9, 1940. He was unconscious for about 24 hours and remained in a hospital elsewhere for three weeks. Three days after leaving the hospital a blood clot was discharged from his left nostril, followed by a profuse flow of clear fluid. Fever appeared the following day, accompanied by chills, but these subsided under sulfathiazole and sulfanilamide therapy. He was readmitted to the hospital and kept on isolation precautions, including masks. In spite of this, pneumococcus meningitis occurred, Dec. 3, 1940; it was rapidly controlled by intravenous sulfapyridine therapy. He continued to receive sulfapyridine, 4 gm. daily, until his transfer to the New Haven Hospital, Jan. 7, 1941.

Examination revealed a large, irregular scar in the midforehead. A few drops of clear fluid could be obtained from the left nostril by appropriate changes in head position. X-rays of the skull demonstrated multiple, small fragments of cortical bone behind the frontal sinuses. The preoperative sulfapyridine blood level was 5.5 mgm. per cent.

Operation: A left frontal osteoplastic bone flap was elevated, disclosing several rough, bony projections on the inner table, apparently representing spicules of bone which had been thrown off from the inner table at the time of injury. The dura was slightly thickened in this region and showed evidences of an old laceration. The dura was opened and the frontal lobe

elevated, revealing a meningocortical scar attaching the inferior surface of the frontal pole to a defect in the bone and dura, 15×10 mm., at the cribriform plate. The meningocortical scar was fulgurated and excised. A dural flap from the falx and crista galli was sutured across the defect, after the application of a small amount of sterile sulfapyridine powder to the defect. At the hinge of the dural graft, a fracture was found at the base of the crista galli. A small muscle graft was tucked under the hinge of the dural flap to cover this fracture line. Small muscle grafts were also inserted beneath the anterior and posterior margins of the dural flap to fill the olfactory groove. Convalescence was uneventful except for two convulsions. Cerebrospinal rhinorrhea has not recurred.

Case 4. (N.H.H. #B16615). A young man of 19 years fell asleep while driving an automobile and received a compound frontal craniocerebral injury when the car struck a tree.

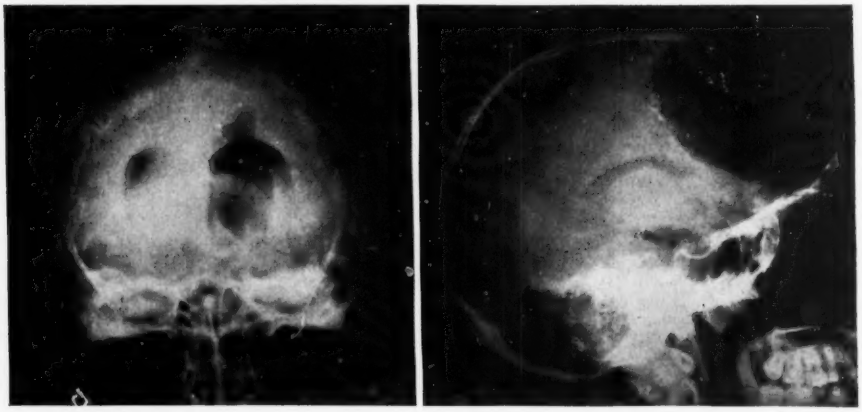


FIG. 2. *Case 4.* Roentgenograms demonstrating stellate fracture in left frontal region and depression of the left orbital roof; air in the ventricular system and within a large left frontal porencephaly.

When admitted to a hospital elsewhere, macerated cerebral tissue was noted, extruding from the left nostril, the left pupil was dilated and he remained unconscious for twenty-four hours. He remained in the hospital twenty-five days and cerebrospinal rhinorrhea was first noted five days after he returned home. Following this there were progressive headache, nausea and vomiting, weakness, intermittent stupor and fever. He was admitted to the New Haven Hospital on July 3, 1941, two months after the accident.

Examination revealed a healed scar at the left supraorbital ridge. The left eye was slightly depressed by downward displacement of the left supraorbital ridge; there was left enophthalmos and the left pupil reacted sluggishly to light; upward gaze was limited on the left. There was bilateral anosmia and clear fluid dripped from the left nostril (total protein: 113 mgm. per cent; cell count: 5). He was confused at times, was unable to walk and made no apparent effort at urinary control. X-rays of the skull (Fig. 2) demonstrated a large, stellate fracture of the left frontal bone, extending downward to the region of the cribriform plate; air was present in both lateral ventricles, a small amount in the third ventricle and over both frontal lobes, apparently in the subdural* and subarchnoid spaces. Sulfapyridine was given preoperatively.

Operation: A left frontal osteoplastic bone flap was elevated and the dura opened along the anterior margin of the exposure, revealing a traumatic porencephaly. The thin covering

* This air was verified at operation in a porencephalic cavity.

membrane was punctured and air escaped, deflating the left frontal lobe, which was then elevated. The inferior surface of the frontal pole was attached by a meningocortical scar to a defect in the cribriform plate. The scar was excised and a large dural defect was found, extending 1.5 cm. lateral to the opening in the cribriform plate. A dural flap from the crista galli and falx was folded over the bone defect and sutured to a second dural flap hinged from the dura of the lateral floor of the anterior fossa. A muscle graft was tucked under the hinge of the lateral dural flap, which tended to pull away from the underlying bone. Sterile sulfathiazole crystals were applied to the bone defect, and the posterior portion of the olfactory groove was filled with a second, small muscle graft. Recurrent cerebrospinal rhinorrhea was noted on several occasions post-operatively but this ceased before his discharge from the hospital and has not recurred. Convalescence was complicated by sterile meningitis and by local infection along the margin of the bone flap, requiring revision of a portion of the wound.

Case 5. (N.H.H. #B17961). A man of 21 received a compound craniocerebral injury in an automobile accident, Mar. 22, 1941. He was unconscious for about three days and was treated in a hospital elsewhere over a period of five weeks. Cerebrospinal rhinorrhea was noted from the right nostril, four weeks after the injury. He was admitted to the New Haven Hospital on July 21, 1941.

Examination disclosed a long crescentic scar above the glabella and a small scar just medial to the right eye. The nose was deviated to the right, the left nostril was partially occluded and anosmia was complete. Clear fluid dripped from the right nostril (total protein: 415 mgm. per cent; cell count: 95 lymphocytes). X-rays of the skull revealed a fracture of the frontal bone, extending into the frontal sinuses. Sulfapyridine was given preoperatively.

Operation: A right frontal osteoplastic bone flap was elevated and the dura opened along the anterior margin of the exposure. The frontal lobe was elevated, exposing a meningocortical scar on the inferior surface of the frontal pole, attached to and wedged into a defect, 1 × .5 cm., in the cribriform plate. A large dural defect was present, lateral to the opening through the cribriform plate. A dural flap was reflected from the crista galli and falx and sutured to the remaining portion of dura. The dural flap was supplemented by a free graft of periosteum, from the bone flap; this was sutured at the margins of the large dural defect and to the edge of the dural flap. A small amount of sterile sulfathiazole powder was placed beneath the flaps and the olfactory groove was filled with a bit of muscle, tucked under the edge of the dural flap. Both olfactory nerves had apparently been completely destroyed at the time of the accident and there was evidence of injury to the left frontal lobe. Convalescence was uneventful but occasional drops of fluid were noted from the right nostril until about one month after operation. The cerebrospinal rhinorrhea ceased at that time and has not recurred.

COMMENT

Local infection along the margin of the bone flap occurred in two instances, attesting to the potential source of contamination in these fistulae. In all cases, operation was preceded and followed by sulfonamide medication. There was no postoperative meningeal infection, though one patient had sterile meningitis, with mild fever and pleocytosis. Delayed cessation of cerebrospinal rhinorrhea occurred in two cases having extensive dural defects; double dural flaps were necessary in these instances (Cases 4 and 5). The four adult patients have resumed normal occupations and there has been no recurrence of cerebrospinal rhinorrhea.

SUMMARY

A method is described for surgical repair of cerebrospinal rhinorrhea utilizing a dural flap from the crista galli and falx to cover the defect in the

cribriform plate. Five cases are presented in which this procedure was used successfully.

REFERENCES

1. Adson, A. W. Cerebrospinal rhinorrhea; surgical repair of fistula: report of a case. *Proc. Mayo Clin.*, 1941, *16:* 385–387. Cerebrospinal rhinorrhea: surgical repair of craniosinus fistula. *Ann. Surg.*, 1941, *114:* 697–705. Results following surgical repair of craniosinus fistula for cerebrospinal rhinorrhea: abstract of a published paper with comment on subsequent experience. *Proc. Mayo Clin.*, 1942, *17:* 281–286.
2. Cairns, H. Injuries of the frontal and ethmoidal sinuses with special reference to cerebrospinal rhinorrhoea and aeroceles. *J. Laryng.*, 1937, *52:* 589–623.
3. Coleman, C. C. Fracture of the skull involving the paranasal sinuses and mastoids. *J. Amer. med. Ass.*, 1937, *109:* 1613–1616.
4. Dandy, W. E. Pneumocephalus (intracranial pneumatocele or aerocele). *Arch. Surg., Chicago,* 1926, *12:* 949–982.
5. Eden, K. Traumatic cerebrospinal rhinorrhoea. Repair of the fistula by a transfrontal intradural operation. *Brit. J. Surg.*, 1942, *29:* 299–303.
6. Gissane, W., and Rank, B. K. Post-traumatic cerebrospinal rhinorrhoea with case report. *Brit. J. Surg.*, 1940, *27:* 717–722.
7. Graham, T. O. Cerebrospinal rhinorrhoea. *J. Laryng.*, 1937, *52:* 344–347.
8. Johnston, W. H. Cerebrospinal rhinorrhea—the study of one case and reports of twenty others collected from the literature published since nineteen hundred. *Ann. Otol., etc., St. Louis,* 1926, *35:* 1205–1240.
9. Munro, D. The modern treatment of craniocerebral injuries with especial reference to the maximum permissible mortality and morbidity. *New Engl. J. Med.*, 1935, *213:* 893–906.
10. Peet, M. M. Symptoms, diagnosis, and treatment of acute cranial and intracranial injuries. *N. Y. St. J. Med.*, 1928, *28:* 555–562.
11. Teachenor, F. R. Intracranial complications of fracture of skull involving frontal sinus. *J. Amer. med. Ass.*, 1927, *88:* 987–989.

THE LUCITE CALVARIUM—A METHOD FOR DIRECT OBSERVATION OF THE BRAIN

I. THE SURGICAL AND LUCITE PROCESSING TECHNIQUES*

LIEUT. C. HUNTER SHELDEN (MC) U.S.N.R., LIEUT. ROBERT H. PUDENZ (MC) U.S.N.R., LT. COMDR. JOSEPH S. RESTARSKI (DC) U.S.N., AND CAPTAIN WINCHELL McK. CRAIG (MC) U.S.N.R.

Naval Medical Research Institute and Neurosurgical Service, Department of Surgery, U. S. Naval Hospital, National Naval Medical Center, Bethesda, Maryland

(Received for publication December 19, 1943)

INTRODUCTION

OBSERVATIONS of the living brain through a cranial window have been periodically reported since Ravina described his original procedure in 1811.[5] With the passage of time improvements in the design of these windows have been instituted according to the nature and duration of the proposed experiments. In the earlier investigations windows were usually devised for temporary emplacement into skull openings. More recently, workers have directed their efforts toward the development of more permanent windows. In this communication a technique is described for the permanent replacement of the convex portion of the skull of experimental animals by a transparent lucite plate.

HISTORICAL BACKGROUND

The window used by Ravina consisted of a hollow wooden tube, one end of which was fixed into a trephine opening in a dog's skull and the other closed by a watch glass. Ravina noted pulsation of the brain synchronous with the cardiac pulse and with respiration. Such movement was obviously made possible by the column of air in the wooden tube.

In 1850, Donders[2] cemented square glass windows into the skull defects of experimental animals with rubber and collodion. The tight seal between the skull and glass effectively maintained the closed box of the intracranial system as evidenced by the lack of cerebral pulsation.

The design of the cranial window was improved considerably by Leyden,[4] who constructed a steel-framed, glass window which was screwed tightly into a skull defect. A small petcock was incorporated in the window to permit the introduction and withdrawal of air and fluids. Using this apparatus Leyden investigated the origin of cerebral pulsation, the mechanism of intracranial pain and the local and general effects of increased intracranial pressure. Many of his findings were apparently lost with the passage of time, and upon being rediscovered, have been accepted as modern contributions.

---

* This article has been released for publication by the division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth in this article are those of the writers and are not to be considered as reflecting the policies of the Navy Department.

The window most extensively used in modern neurophysiological procedures is undoubtedly the one described by Forbes[3] in 1928. At this time he reported the first of a series of acute experiments in which the diameters of the pial vessels were measured under various conditions. Forbes' window is constructed of a circular piece of glass, 18 mm. in diameter, which is cemented to a steel frame. The latter is beveled and threaded at the edge so that it can be screwed tightly into a skull aperture. Hypodermic needles of 17 gauge are soldered into the steel frame for the injection and aspiration of fluids and gases.

Permanent cranial windows have been devised by Wentsler[7] and by Sohler, Lothrop and Forbes.[6] The former apparatus consists of a small glass window set into a celluloid frame which is secured to the skull with fine, silver pegs. In a more recent communication, Clark and Wentsler[1] stated that this type of window had been installed in two rabbits. In the first animal the area became infected and the window dropped out in approximately five months. In the second rabbit the window was still in perfect position nine months following operation.

The permanent windows of Sohler and his colleagues have been fabricated from lucite discs. These windows are screwed into skull defects by means of threaded, beveled edges. Two small holes are incorporated for the introduction and removal of fluids and gases. Optically polished surfaces enable the observer to study the cerebral circulation with a microscope. The disadvantage of this type of lucite window is its small size, namely, a diameter of either 12 or 16 millimeters.

Interest in the direct observation of intracranial phenomena resulting from head trauma led to the attempt to develop a cranial window of large enough size to permit visualization of both cerebral hemispheres simultaneously. Efforts directed toward this end resulted in the development of the lucite calvarium described herein. The term "calvarium" is used to distinguish this window from those described previously, all of which are small in size.

Monkeys with lucite plates are being used to investigate the intracranial changes associated with blows on the head. The pattern of motion of the cerebral mass under various traumatic conditions is clearly visualized with high speed cinematography. In addition to this study of head injury, the lucite preparations are being employed to study the intracranial phenomena resulting from exposure to high and low barometric pressures, oxygen poisoning, pressure breathing and the administration of drugs. The reports of the findings in these investigations will be forthcoming. In this communication the surgical technique and the method of processing the lucite plate are presented.

METHODS AND MATERIALS

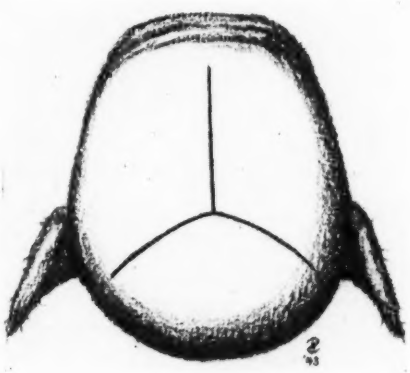
Macacus rhesus monkeys have been used in all of the experiments. The technique leading to a successful preparation of a lucite calvarium is divided into four stages:

1. The first stage of operation.
2. The lucite processing technique.
3. The second stage of operation.
4. Post-operative care.

Each of these stages is discussed separately.

1. *The First Stage of Operation.* To insure cleanliness the monkey is bathed in soap and water and placed in a clean cage. At the time of operation the animal is anesthetized with sodium pentobarbital intraperitoneally in doses of 32 mgm. per kilogram. The head is firmly fixed in a special holder, shaved, and cleansed with green soap. Layers of alcohol, ether and tincture of merthiolate are applied and the operative field is draped with sterile towels.

A Y-shaped incision is used (Fig. 1). The anterior limb of this incision extends in the mid-



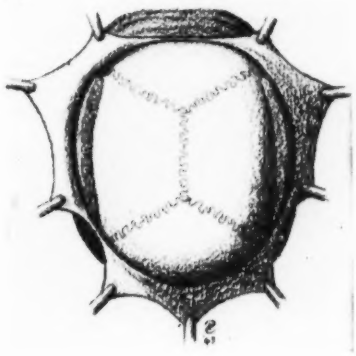
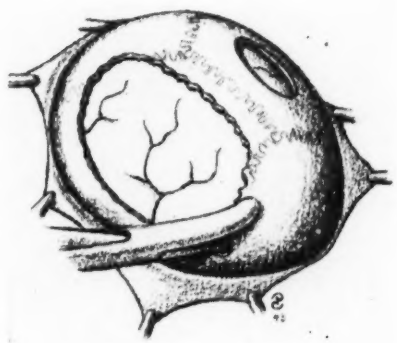


FIG. 1 (*left*). The Y-shaped incision.

FIG. 2 (*right*). Convexity of skull is exposed after removal of muscle and periosteum. The cut edges of both temporal muscles are shown.



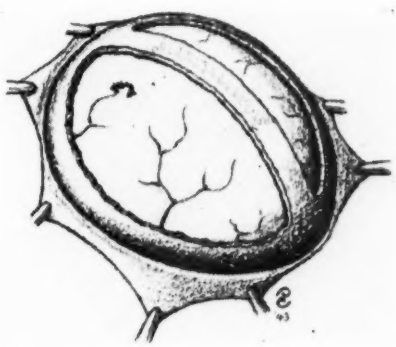


FIG. 3 (*left*). Trephine opening on right. Removal of bone with rongeurs on left.

FIG. 4 (*right*). The bilateral skull defects are shown. Note the strip of bone maintaining fixation of the longitudinal sinus and the falx cerebri.

line from a point 2 centimeters above the supraorbital ridge posteriorly to the lambdoidal suture. From this latter point the incision curves postero-laterally on both sides paralleling the lambdoidal suture. This three-limbed incision is preferable to a cross type which allows too much subsequent recession of the scalp margin.

After reflecting the scalp, the periosteum and the upper portions of both temporal muscles are removed. This is accomplished by incising these tissues peripherally with the electrocautery and stripping with a periosteal elevator (Fig. 2). It is essential to remove all of the periosteum. If this is not done the small adherent fragments of tissue will interfere with the hydrocolloid impression.

A burr hole is placed in each lateral parietal area and enlarged until the desired defects in the bone are obtained (Fig. 3). A midline section of bone is left to maintain fixation of the falx cerebri as well as to retain the continuity of the longitudinal sinus (Fig. 4). The dura is left undisturbed to cover the cortex.

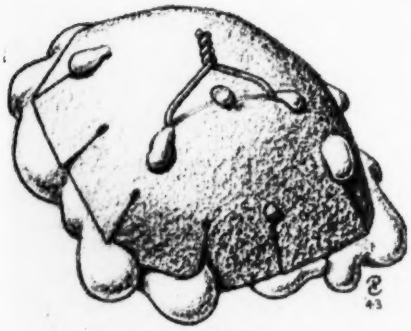


FIG. 5. Hydrocolloid impression of the skull.

At this point an impression of the bony defects is made in hydrocolloid. Care is taken to ensure adequate exposure so that the hydrocolloidal material will overlap the skull for at least 1 centimeter beyond the defects (Fig. 5). The scalp is closed without drainage. A gauze dressing is applied and held in place with liquid adhesive. Further protection of the wound is obtained by placing a rubberized helmet over the dressing and securing it with strings tied under the chin.

2. *The Lucite Processing Technique.*

(a) *The Impression:* The ultimate fit of the lucite calvarium is largely dependent on the initial impression of the area to be covered. Any good hydrocolloidal impression material is satisfactory for this purpose. Hydrocolloids are sterilizable and workable at temperatures tolerated by the intracranial tissues.

Before taking an impression, it is necessary to construct a well-fitting impression tray. Sheet copper or aluminum, 1 mm. in thickness, is excellent for this purpose. A tray made from either metal may be contoured and reshaped for use in subsequent operations. A stout wire loop attached to the outer surface of the tray aids in removing the impression from the skull. The value of a properly constructed impression tray cannot be overemphasized. Unless the hydrocolloid is properly confined, the impression will be inaccurate and the completed lucite plate will not fit. The tray should extend at least 1 cm. beyond the margins of skull defects to ensure a good seal at the skull-lucite junction.

(b) *The Stone Working Model:* When an accurate impression is obtained the stone model of the skull (Fig. 6) should be made without delay. Any dental stone of good quality may be used. Should it be necessary to delay the construction of the stone model, the impression may be kept until the following day if it is carefully wrapped in moistened gauze and kept in a damp place. If allowed to dry the hydrocolloid will shrink and warp.

(c) *Waxing Technique:* When the stone model hardens it is separated from the impression. A wax plate, which is eventually duplicated in lucite, is constructed on the stone model. Standard dental base-plate wax is well suited for this purpose. Enough wax is used to give the plate a thickness of about 2 mm. An excess of 1 mm. is applied at points where holes are to be made for drainage and for attachment of the plate to the skull with the metal screws (Fig. 7).

(d) *Constructing the Mold:* A standard sectional denture flask is used in making the mold for processing the lucite. The lower half of the flask is filled with a mixture of dental stone and plaster of Paris in equal parts. While this mixture is still soft, the wax-covered stone model

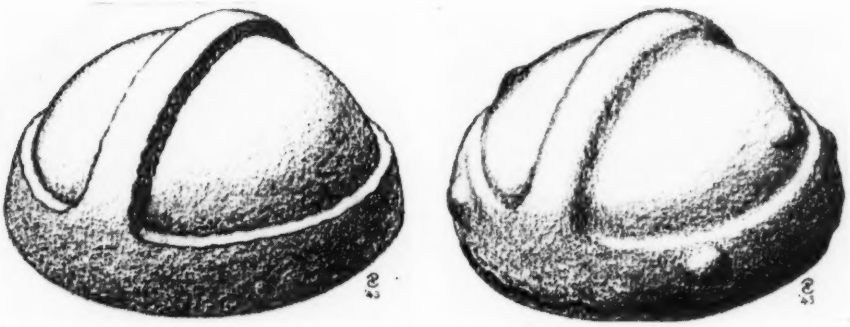


FIG. 6 (*left*). Model of the skull fabricated from dental stone.
FIG. 7 (*right*). Wax model of the cranial plate. Excess wax is applied at points where screws will be inserted.

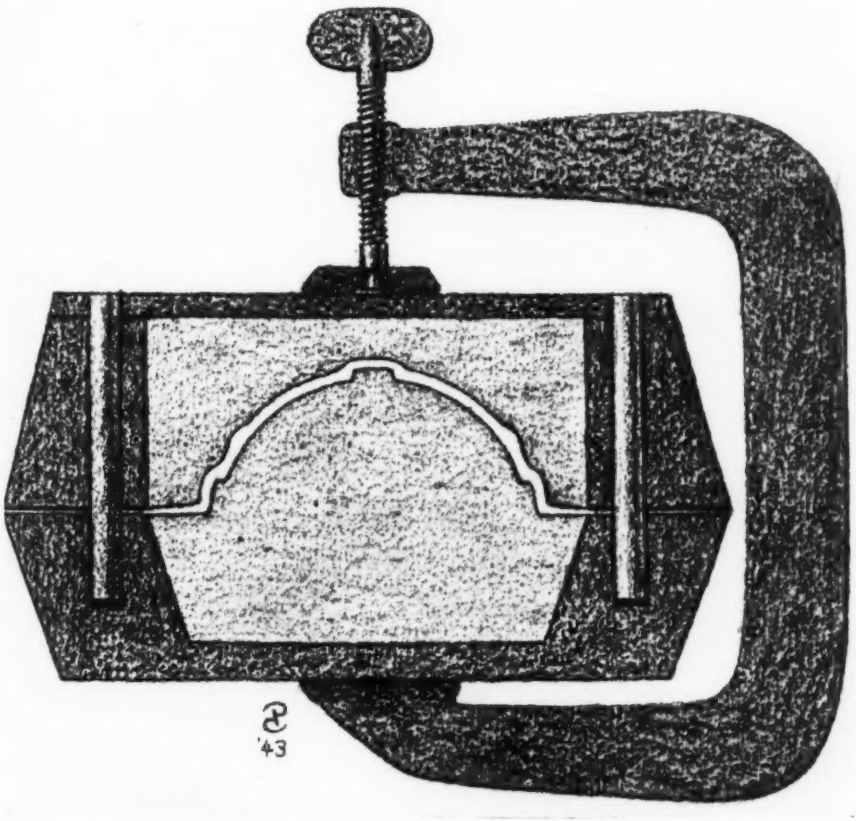


FIG. 8. Cross section of mold showing space lined with tin foil and filled with lucite.

FIG. 9. Lucite calvarium attached to skull with four screws. The two drainage holes are closed with brass screws.

is embedded in the mass allowing the plaster to just cover the margin of the wax. After the plaster mass hardens all of its exposed surfaces are covered with a film of soap. The soap acts as a separating medium. Following this step the upper half of the flask is filled with a similar plaster mix which is also allowed to harden. The flask is closed and immersed in boiling water for ten minutes. The heat melts out the wax thereby preparing the cavity to be filled with lucite. This space is lined with 0.001 gauge tin foil to prevent seepage of the lucite into the pores of the plaster. The metal lining assures a hard clear finished product.

(e) *Processing the Lucite:* Lucite is polymerized methyl methacrylate. The actual processing of this material is a simple process and requires no special apparatus. Three parts of powdered lucite are placed in a clean glass beaker and one part of liquid methyl methacrylate monomer added. This mixture should stand for at least ten minutes. In the meantime the mold is heated to approximately 150° Fahrenheit by placing the separated upper and lower sections in a shallow water bath for approximately one-half hour. Care should be taken to prevent the hot water from contacting the tin foil otherwise separation from the plaster will result. By the time the mold is satisfactorily heated, the lucite mixture will have formed a jelly-like, opalescent mass. This consistence is necessary for obtaining proper compression of the lucite when the mold is closed.

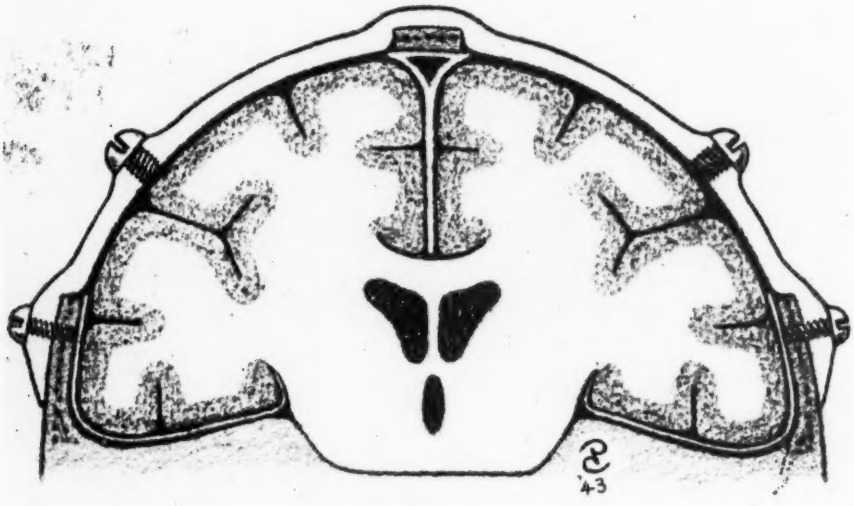


FIG. 10. Cross section showing relation of the plate to the skull, brain and dura.

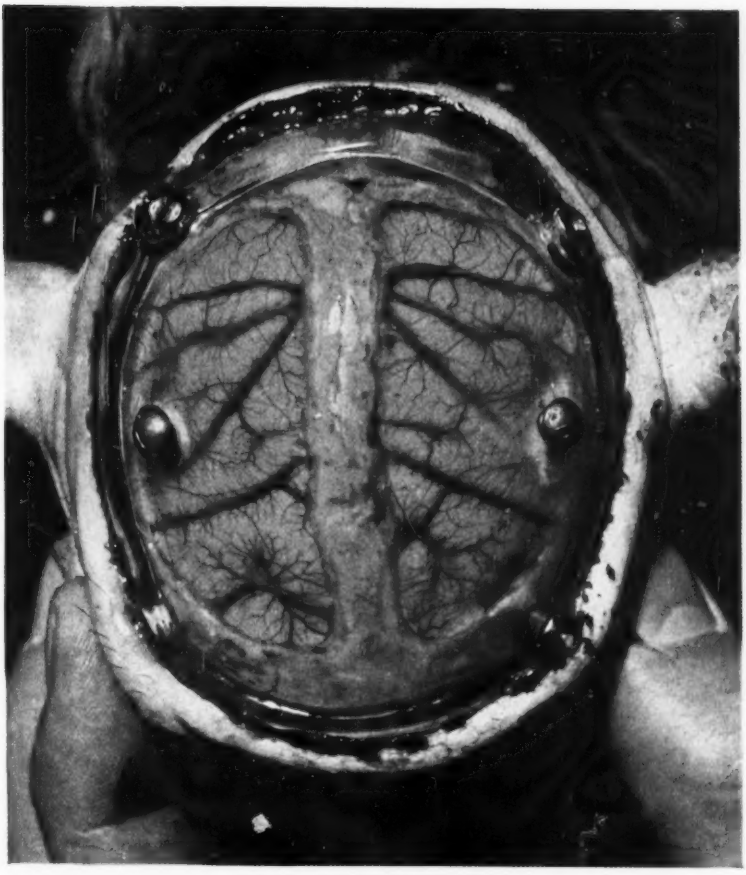


FIG. 11. Color photograph showing the characteristic view as seen through a lucite calvarium. Photograph taken 10 days following attachment of the plate.

After placing the lucite in the mold the latter is inserted into a mechanical press and closed slowly. The gradual application of pressure causes the excess material to escape, permits complete closure of the mold and results in the desired degree of compression of the lucite mixture. When the closure is completed the mold is placed in boiling water for 45 minutes to cure the lucite. A cross section of the mold containing the lucite mixture is shown in Fig. 8. Following removal the mold is allowed to cool thoroughly before removing the lucite plate.

The tin foil is peeled away with but little difficulty. Adherent pieces are ground away with dental burrs and stones. Finishing and polishing are done with revolving stones and wet pumice. The final high luster is obtained with wet whiting on a high-speed rag wheel.

3. *Second Stage of Operation.* After an interval of three to five days the wound is reopened and prepared for the application of the lucite plate. Bleeding from the bone is controlled with Horsley's wax. The dura is removed bilaterally and all bleeding points electrocoagulated. The lucite plate, which has been thoroughly washed with soap and water and cold sterilized in a 1:1000 mercuric chloride solution, is fitted to the skull. Small holes for insertion of the screws are drilled in the skull at points corresponding to holes previously placed in the flange of the plate. Firm fixation of the lucite calvarium to the skull is obtained by four stout $\frac{1}{4}$" tantalum or vitallium screws (Figs. 9 and 10). The characteristic view of the brain as seen through the lucite calvarium is shown in color in Fig. 11.

The three limbs of the scalp incision are sutured to points just above the flange of the plate. The remainder of the scalp is resected thereby leaving the midportion of the lucite calvarium uncovered. Sterile gauze dressings are applied.

4. *Post-operative Care.* Certain problems must be given careful attention in the immediate post-operative period to ensure a satisfactory preparation. Drainage of the "subdural" space is essential to prevent post-operative clouding beneath the plate. This is accomplished by removing the small brass screws in the drainage holes to permit the escape of the xanthochromic fluid that has collected. At the end of three to five days the screws are sterilized and replaced. Dressings are changed periodically during the first two weeks, after which time no further protection is necessary.

RESULTS

Of the 14 monkeys (L1–L14) prepared up to the present time, only the last 4 have had the procedure carried out according to the technique outlined in the previous section. The first 10 animals were used in the development of the method. Many difficulties were encountered, the outstanding of which were the clouding of the cerebral surfaces due to the deposition of fibrin on the leptomeninges, the obtaining of a secure fit of the plate to prevent leakage of cerebrospinal fluid, and the proper treatment of the skin.

The formation of the filmy layer of fibrin over the surface of the brain has been prevented by meticulous hemostasis of the dura and bone and by drainage of the "subdural" space for several days following the second stage of operation. Daily irrigation of this space proved unsatisfactory. Although the irrigation removed the xanthochromic fluid, it was followed in several instances by a mixed type of infection which ruined the preparation.

The present model of the lucite plate, which has a 1 cm. flange and which is screwed, rather than wired, to the skull, permits a secure attachment. Moderately severe blows (velocity of 30 feet per second and energy of 6.6 foot pounds) delivered to the animals' heads have not resulted in a cerebrospinal fluid leak. Furthermore, no leak of cerebrospinal fluid occurred when the monkeys were exposed to barometric pressures varying from 1/5 of an atmosphere to 5 atmospheres.

Infection of the skin has been a minor problem. Within a few weeks the skin edge recedes below the margin of the plate, curls inward and adheres to the temporal muscles and pericranium. Efforts to promote adherence of the skin to the plate by incorporating a rim of tantalum in the flange have failed. Suturing the skin to the plate with tantalum wire was also unsuccessful and has been abandoned.

Since adopting the use of the wide flange, attachment of the plate with screws and post-operative drainage, the cerebral surfaces have remained clear for considerable periods of time. Prior to the infliction of trauma on the 29th post-operative day the cerebral vascular pattern of monkey L11 was distinctly visible and the diameters of the vessels could be measured with a dissecting microscope. Similarly, the brains of animals L12 and L13 remained clear until the one animal died of aeroembolism following decompression on the 18th post-operative day, and the other was subjected to cranial trauma, leading to bilateral subdural and subpial hemorrhage on the 10th post-operative day. Within three weeks these hemorrhages were absorbed and the circulatory pattern was again clearly visible. Monkey L14, the most recent preparation, is being used for various studies at the present time.

Repeated observations of these animals have disclosed no behavior difficulties following the attachment of the lucite calvarium. A few of the animals pick at the plate but most appear entirely unconcerned. Furthermore, although detailed examinations have not been made, there have been no disturbances suggestive of gross cerebral damage.

DISCUSSION

From the detailed descriptions of the technical stages one may gain the impression that this is a complicated and time-consuming procedure. On the contrary, the technique requires only the observance of basic neurosurgical principles and the availability of facilities and materials found in any dental laboratory. Furthermore, the operative procedures and the lucite processing technique are not unduly lengthy. The total time expended by both stages of the operation is less than two hours. The processing of the lucite plate demands approximately $1\frac{1}{2}$ hours of working time.

In our hands, the following steps are considered most essential to obtain a satisfactory preparation:

1. An accurate hydrocolloid impression so that the lucite plate will completely fill the bilateral defects and overlap the surrounding skull for at least 1 centimeter.

2. Meticulous control of all bleeding from the cut edges of the bone and dura.

3. Drainage of the "subdural" space for 3 to 5 days following the second stage of operation.

Although minor technical improvements are being constantly introduced, the method as outlined has proved eminently satisfactory for our purpose.

SUMMARY AND CONCLUSIONS

1. A technique for the permanent substitution of the calvarium of monkeys with a transparent lucite plate is described.

2. The lucite plate, due to its configuration to the apertures in the bone and to the surrounding skull, maintains intracranial hydrodynamics and presents an extensive view of both cerebral hemispheres.

3. The lucite technique is adaptable to the study of a wide variety of intracranial phenomena.

The technical assistance of J. G. Wisda, PhM2c U.S.N.R. is gratefully acknowledged.

REFERENCES

1. Clark, E. R., and Wentsler, N. E. Pial circulation studied by long-continued direct inspection. *Res. Publ. Ass. nerv. ment. Dis.*, 1937, *18:* 218–228.
2. Donders, F. C. Die Bewegungen des Gehirns und die Veränderungen der Gefässfüllung der Pia mater, auch bei geschlossenem, unausdehnbarem Schädel unmittelbar beobachtet. *Schmidts Jb.*, 1851, *69:* 16–20.
3. Forbes, H. S. The cerebral circulation. I. Observation and measurement of pial vessels. *Arch. Neurol. Psychiat., Chicago*, 1928, *19:* 751–761.
4. Leyden, E. Beiträge und Untersuchungen zur Physiologie und Pathologie des Gehirns. *Virchows Arch.*, 1866, *37:* 519–559.
5. Ravina, A. F. Quoted by Forbes[3].
6. Sohler, T. P., Lothrop, G. N., and Forbes, H. S. The pial circulation of normal, non-anesthetized animals. Part 1. Description of a method of observation. *J. Pharmacol.*, 1941, *71:* 325–330.
7. Wentsler, N. E. Microscopic study of the superficial cerebral vessels of the rabbit by means of a permanently installed transparent cranial chamber. *Anat. Rec.*, 1936, *66:* 423–435.

THE CHEMOTHERAPY OF INTRACRANIAL INFECTIONS

IV. THE TREATMENT OF PNEUMOCOCCAL MENINGITIS BY INTRATHECAL ADMINISTRATION OF PENICILLIN*

COBB PILCHER, M.D. AND WILLIAM F. MEACHAM, M.D.
Department of Surgery, Vanderbilt University School of Medicine, Nashville, Tennessee

(Received for publication December 21, 1943)

IN A PREVIOUS STUDY,[1] penicillin administered intrathecally, even in relatively small doses, was found to be beneficial in experimental staphylococcal meningitis in dogs. We wish here to report a similar study of meningitis due to the pneumococcus, Type I.

A virulent strain of this organism was inoculated into the cerebrospinal fluid of a number of successive dogs until the resulting meningitis was relatively consistent in its course, nearly always terminating fatally in two to seven days, with viscid, grossly purulent cerebrospinal fluid. A large amount of an eighteen-hour culture of the organism (in saline suspension) was then sealed in sterile glass ampoules and preserved in the frozen state, as with the cultures of staphylococci previously reported.[1]

Meningitis was produced in a number of groups of ten to fourteen dogs by injection of approximately 3,000,000 pneumococci into the cisterna magna. Half of each group of animals was treated, the remaining half was used as controls. Daily (or more frequent) cultures of blood and cerebrospinal fluid were made, clinical observations were recorded and necropsy was carried out at the termination of all experiments. Histologic studies were made on most animals. Surviving animals were sacrificed only after cultures had been sterile and symptoms absent for at least ten days.

RESULTS

Control experiments were strikingly similar in most groups. Only two of forty-six control animals recovered (4.3 per cent). Death occurred within three days (usually on the third day) in nearly half and from three to seven days (usually on the fourth or fifth days) in nearly all the remainder.

In the first series of 48 experiments, divided into four groups, intracisternal injection of 50 units† of penicillin (dissolved in 1 c.c. of saline solution) twice daily was the therapy employed (Fig. 1). In each of the four groups, results

* The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Vanderbilt University. The penicillin was furnished by E. R. Squibb and Sons and by Charles Pfizer, Inc., New York, on recommendation of the Committee on Chemotherapeutic and Other Agents of the National Research Council.

† This very small dosage was employed partly because very little penicillin was available to us at the time and partly because it seemed advantageous nevertheless to determine the effects of the same minimal dosage employed in previous experiments on staphylococcal meningitis.

were slightly but definitely more favorable in the treated than in the untreated animals. Of 22 untreated dogs, only one survived, whereas four of 26 treated dogs recovered. Furthermore, the incidence of early death was distinctly higher among the control animals.

In the next two groups of 12 dogs each, treatment consisted of intracisternal administration of 100 and 200 units of penicillin, respectively, twice

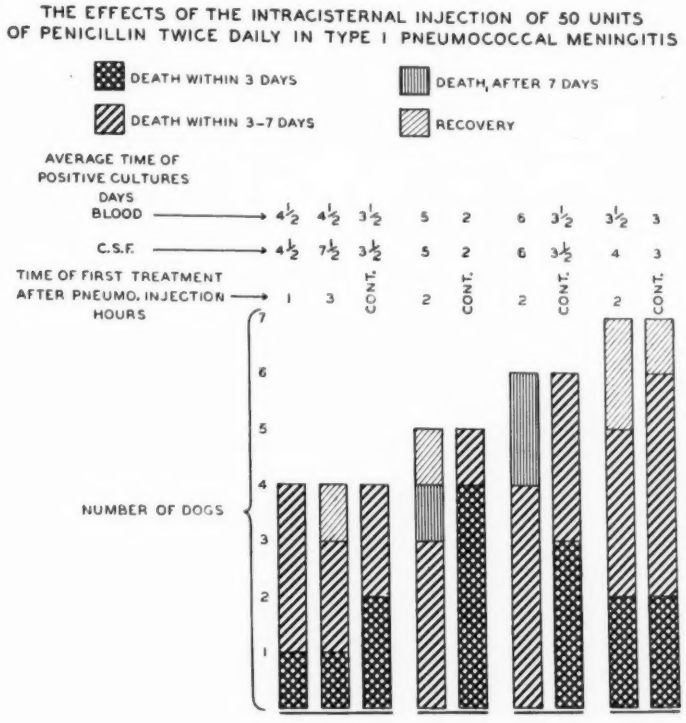

THE EFFECTS OF THE INTRACISTERNAL INJECTION OF 50 UNITS OF PENICILLIN TWICE DAILY IN TYPE I PNEUMOCOCCAL MENINGITIS
DEATH WITHIN 3 DAYS
DEATH, AFTER 7 DAYS
DEATH WITHIN 3–7 DAYS
RECOVERY
AVERAGE TIME OF POSITIVE CULTURES
DAYS
BLOOD
C.S.F.
TIME OF FIRST TREATMENT AFTER PNEUMO. INJECTION HOURS
NUMBER OF DOGS
CONT.

FIG. 1

daily (Fig. 2). One treated animal is not included in the chart because a positive culture was not obtained in the cerebrospinal fluid at any time in a period of 12 days and it was thought possible that the organisms had been injected epidurally.

Among the twelve control animals, only one survived, whereas five of the eleven treated dogs recovered.

It was observed in these groups that the cerebrospinal fluid of all treated animals was grossly clear with a very moderate pleocytosis, whereas in the control dogs, the fluid was invariably grossly purulent and frequently so viscid that only small specimens could be obtained by cisternal puncture

(Fig. 3). This observation was confirmed at necropsy. Furthermore, the blood cultures of the treated animals invariably were positive for the pneumococcus and frequently remained so for some days (Fig. 2). At necropsy most of the treated animals that failed to survive were found to have lobar pneumonia from which the pneumococcus could be recovered.

Since the gradual absorption of the small and infrequent intrathecal doses

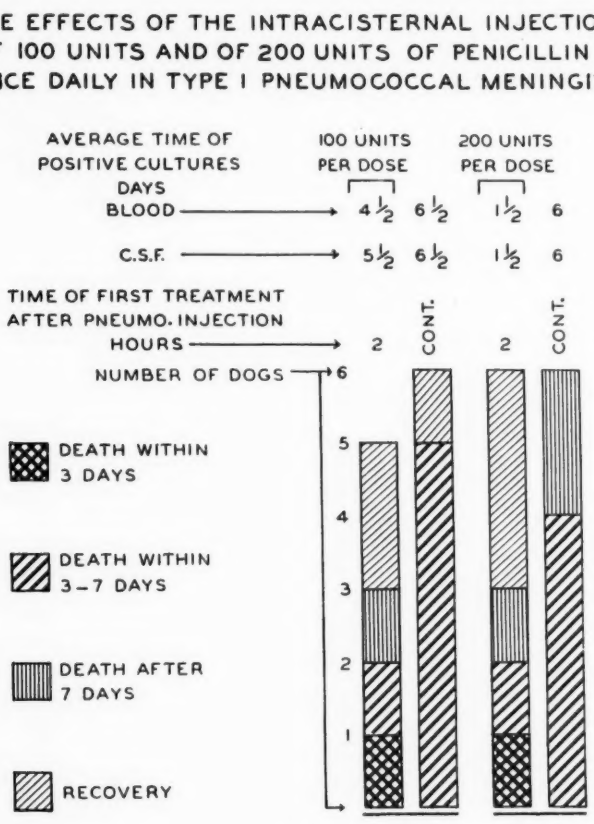


FIG. 2

of penicillin could not be expected to produce a therapeutically significant blood level of the drug, it seemed likely that pneumonia was responsible for many of the deaths among the treated animals. That this was not equally true in the control experiments was evidenced by the grossly purulent cerebrospinal fluid and post-mortem histological evidence of severe and extensive meningitis in these animals.

In order to obviate the factor of pneumonia as far as possible, two addi-

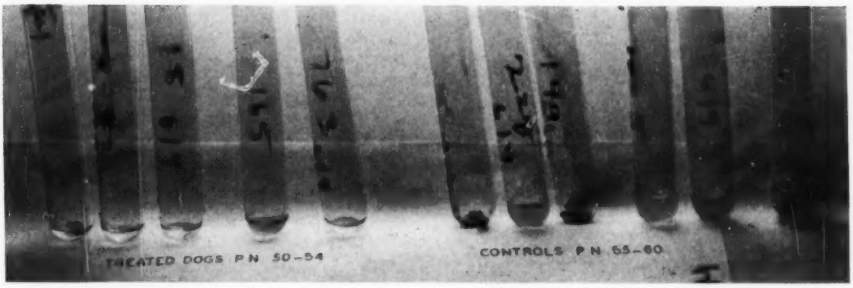


FIG. 3. Specimens of cerebrospinal fluid obtained from simultaneously infected groups of treated and untreated animals three days after infection. Treatment consisted of intracisternal injection of 200 units of penicillin twice daily.

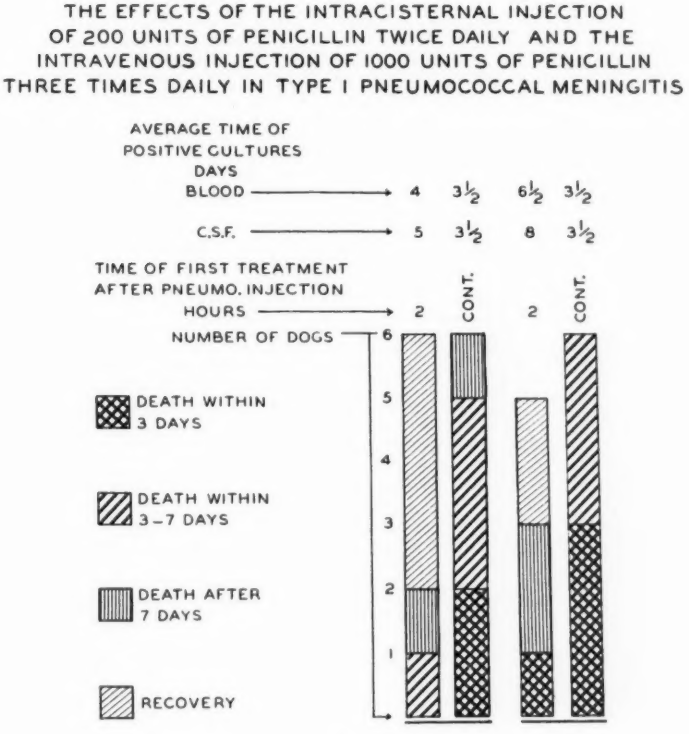


FIG. 4

TREATED DOGS PN 87–90 CONTROLS 91–95

FIG. 5. Specimens of cerebrospinal fluid obtained from simultaneously infected groups of treated and untreated animals two days after infection. Treatment consisted of intracisternal injection of 200 units of penicillin twice daily and intravenous injection of 1000 units of penicillin three times daily.

tional groups of dogs were treated by intrathecal injection of 200 units of penicillin twice daily and intraveneous injection of 1000 units of penicillin three times daily. All injections were spaced approximately evenly in each 24 hours.

In these 24 experiments, the results in the treated animals were even more strikingly favorable (Fig. 4). No control animal recovered, as compared

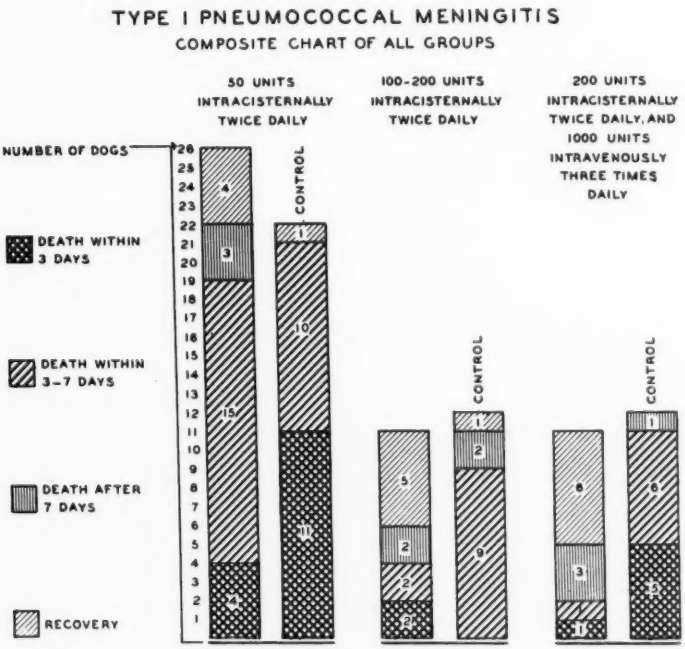


FIG. 6

with six recoveries among the treated dogs.* Five control dogs did not survive three days and six control dogs died in the three-to-seven day period On the other hand, only one treated dog died within three days and only one other in the three-to-seven day period.

In these animals, as in the previous groups, the cerebrospinal fluid presented a striking contrast in the treated and untreated groups (Fig. 5).

COMMENT

Composite results of all the experiments herein reported are shown in Fig. 6.

Despite the relatively small number of experiments (ninety-six) and the difficulty of statistical analysis in experiments designed to simulate clinical conditions, the results of this study indicate clearly that the intrathecal injection of penicillin was of marked benefit under these experimental conditions. They also indicate that intravenous or intramuscular administrations of penicillin should not be neglected when intrathecal therapy is being employed.

Although pneumococcal meningitis sometimes responds favorably to some of the sulfonamides when administered systemically, penicillin offers the additional advantage of an effective chemotherapeutic agent which may be injected intrathecally. In this manner a very high concentration may safely be maintained at the site of infection.

The amounts of penicillin employed in these experiments should not be taken as a guide to dosage in human beings. Penicillin may produce a moderately severe irritative meningeal reaction when injected intrathecally,[1] but Rammelkamp and Keefer[2] have injected as much as 10,000 units into the lumbar subarachnoid space in normal men without serious after-effects. Similarly, intravenous and intramuscular dosage should be much larger and more frequent than in these experiments.

SUMMARY

The effects of intrathecal administration of penicillin in Type I pneumococcal meningitis have been studied in 96 experiments on dogs.

This method of therapy, even with small dosage, was found to reduce the mortality rate and prolong the survival time.

The beneficial effects of intrathecal therapy were markedly increased by the addition of the intravenous administration of penicillin (since secondary infection of the blood stream was invariably present and lobar pneumonia frequently developed if intravenous therapy were not employed).

REFERENCES

1. Pilcher, C., and Meacham, W. F. The chemotherapy of intracranial infections. III. The treatment of experimental staphylococcic meningitis with intrathecal administration of penicillin. *J. Amer. med. Ass.*, 1943, *123:* 330–332.

2. Rammelkamp, C. H., and Keefer, C. S. The absorption, excretion and toxicity of penicillin administered by intrathecal injection. *Amer. J. med. Sci.*, 1943, *205:* 342–350.

* One additional treated dog, apparently recovering, after repeated negative cultures, was sacrificed and discarded because of suspected rabies.

BOOKS YOU OUGHT TO HAVE

Bailey: INTRACRANIAL TUMORS ..... $ 6.00

Crile & Shively: THE HOSPITAL CARE OF THE SURGICAL PATIENT 2.50

Cushing: INTRACRANIAL TUMORS 5.00

Cushing: PITUITARY BODY, HYPOTHALAMUS AND PARASYMPATHETIC NERVOUS SYSTEM 5.00

Cushing & Eisenhardt: THE MENINGIOMAS 15.00

Harvey Cushing Society: A BIBLIOGRAPHY OF THE WRITINGS OF HARVEY CUSHING (2nd Edition) 4.00

Harvey Cushing Society: HARVEY CUSHING'S 70TH BIRTHDAY PARTY (Deluxe edition $5.00) 3.00

Dandy: BENIGN TUMORS IN THE THIRD VENTRICLE OF THE BRAIN 5.00

Dayton: NEW FACTS ON MENTAL DISORDERS 4.50

Ford: DISEASES OF THE NERVOUS SYSTEM IN INFANCY, CHILDHOOD AND ADOLESCENCE (2nd Edition) 10.50

Freeman & Watts: PSYCHOSURGERY 6.00

Fulton & Keller: The Sign of Babinski: A STUDY OF THE CORTICAL DOMINANCE IN PRIMATES 2.00

Grinker: NEUROLOGY (3rd Edition) 7.00

Hamby: THE HOSPITAL CARE OF NEUROSURGICAL PATIENTS 2.00

Kanner: CHILD PSYCHIATRY (3rd Printing) 6.00

Kopeloff: BACTERIOLOGY IN NEUROPSYCHIATRY 4.50

McLellan: THE NEUROGENIC BLADDER 4.00

Nash: SURGICAL PHYSIOLOGY 6.00

Page: CHEMISTRY OF THE BRAIN 7.50

Pancoast, Pendergrass & Schaeffer: THE HEAD AND NECK IN ROENTGEN DIAGNOSIS 6.50

Penfield & Erickson: EPILEPSY AND CEREBRAL LOCALIZATION 8.00

Rand: THE NEUROSURGICAL PATIENT: His Problems of Diagnosis and Care 4.00

Ruch: BIBLIOGRAPHIA PRIMATOLOGICA 8.50

Sladen: PSYCHIATRY AND THE WAR 5.00

Spurling: PRACTICAL NEUROLOGICAL DIAGNOSIS (3rd Edition) 4.00

Winternitz, Thomas & LeCompte: THE BIOLOGY OF ARTERIOSCLEROSIS 4.00

JOURNAL OF NEUROPHYSIOLOGY: (Issued bi-monthly. U.S., Canada & Latin America, $6.00 per year; other countries $6.50)

Order from CHARLES C THOMAS, PUBLISHER · Springfield · Illinois

JOURNAL OF NEUROSURGERY

SCOPE:

The *Journal of Neurosurgery* is devoted to the prompt publication of work relating primarily to neurosurgery, including studies in clinical neurophysiology, and those phases of organic neurology, ophthalmology, radiology and pathology that bear upon the specialized field of neurological surgery. Short articles on neurosurgical technique, special instruments or equipment that might be useful to others in the field, are also acceptable.

MANUSCRIPTS:

Manuscripts for publication should be sent to Dr. Louise Eisenhardt, 310 Cedar Street, New Haven 11, Connecticut, U.S.A. They should be typewritten in double space, with tabular matter and passages for small print in double space on *separate* sheets. All materials should be mailed flat. Books for review and correspondence relating to editorial matters should also be sent to Dr. Eisenhardt.

REFERENCES:

References should be arranged in alphabetical order and typewritten in double space. They should conform to the style used in *A world list of scientific periodicals published in the years 1900–1933* (Oxford University Press, 1934). This requires name(s) and initial(s) of the author(s) with full title and pagination of the paper or book. References should be cited in the text by superior numerals.

ILLUSTRATIONS:

The allowance for free illustrations varies with the length of the paper and the character of the illustrative matter, but not more than four 3×3.5 inch halftones (or equivalent) will be allowed free to any contributor. All illustrations, especially photographs, should be sharp and clear and submitted ready for publication, *i.e.*, with lettering, arrangement, and mounting of figures completed, Illustrations in excess of the free allowance will be charged to the author at a rate of about $5.00 for a 3×3.5 inch halftone, and somewhat less for zinc cuts. Color plates are inserted at the expense of the contributor.

SPECIAL TYPOGRAPHY:

Tables and also text set up in small print (9-point) in excess of 10 per cent of composition costs are charged to the author.

PROOF CORRECTIONS:

Corrections in galley proof will be allowed without charge up to 5 per cent of the original cost of composition of 11-point type. The cost of changes in page proof, if made by the author, will be borne by him. *Page proof will be submitted to authors only when special questions arise.* Manuscripts and figures will be returned after the editorial office has corrected page proof.

REPRINTS:

Owing to the acute shortage of paper it will not be possible to issue gratis reprints to authors, and for the duration of the war large reprint orders must be discouraged. A schedule of charges for reprints will be noted on forms accompanying the galley proof of each paper.

SUBSCRIPTIONS:

The subscription rate for the volume of six bi-monthly issues is $7.50 in the United States, Canada and Latin America, and $8.00 in other countries. Single copies are $1.50 postpaid. Volume I, Number 1 is supplied only on orders for the complete volume. Payments may be made in advance to the publisher Charles C Thomas, 220 East Monroe Street, Springfield, Illinois, U.S.A.

Delivery to countries in war zones will be attempted but delivery is not guaranteed, nor is replacement guaranteed, unless request is received following a period of sixty days after the publication of any issue.

CONTENTS

1. Some of Harvey Cushing's Contributions to Neurological Surgery. GILBERT HORRAX 3

2. The Use of Products Prepared from Human Fibrinogen and Human Thrombin in Neurosurgery. Fibrin Foams as Hemostatic Agents; Fibrin Films in Repair of Dural Defects and in Prevention of Meningocerebral Adhesions. FRANC D. INGRAHAM AND ORVILLE T. BAILEY 23

3. Radiographic Control for Paravertebral Injection of Alcohol in Angina Pectoris. JAMES C. WHITE AND ROBERT W. GENTRY . . . 40

4. Multiple Meningiomas. Report of Two Cases. JOSEPH A. MUFSON AND LEO M. DAVIDOFF 45

5. A Perforator and Ball Burr. KENNETH G. MCKENZIE 58

6. Cerebrospinal Rhinorrhea—Surgical Repair. WILLIAM J. GERMAN . 60

7. The Lucite Calvarium—A Method for Direct Observation of the Brain. I. The Surgical and Lucite Processing Techniques. C. HUNTER SHELDEN, ROBERT H. PUDENZ, JOSEPH S. RESTARSKI, AND WINCHELL MCK. CRAIG 67

8. The Chemotherapy of Intracranial Infections. IV. The Treatment of Pneumococcal Meningitis by Intrathecal Administration of Penicillin. COBB PILCHER AND WILLIAM F. MEACHAM 76

GEORGE BANTA PUBLISHING COMPANY, MENASHA, WISCONSIN

JOURNAL OF NEUROSURGERY

DEDICATION OF THE CUSHING GENERAL HOSPITAL FRAMINGHAM, MASSACHUSETTS 24 JANUARY 1944*

PROGRAM

Master of Ceremonies: Lt. Colonel Henry P. Dunbar
District Engineer, Boston District

INTRODUCTION OF DISTINGUISHED GUESTS
Colonel Dunbar

GREETINGS OF THE COMMONWEALTH OF MASSACHUSETTS
His Excellency Leverett Saltonstall, *the Governor*

ADDRESS
Major General Sherman Miles, *Commanding General, First Service Command*

PRESENTATION OF THE HOSPITAL TO THE MEDICAL DEPARTMENT, U. S. ARMY
Colonel George W. Gillette, *Division Engineer, New England Division*

ACCEPTANCE OF THE HOSPITAL AND PRESENTATION TO THE COMMANDING OFFICER
Brigadier-General Fred W. Rankin, *Representing the Surgeon General*

ACCEPTANCE OF THE HOSPITAL BY THE COMMANDING OFFICER
Colonel Edward A. Noyes, *Commanding Officer*

DEDICATORY ADDRESS
Dr. John F. Fulton, *Sterling Professor of Physiology, Yale University*

INTRODUCTION OF DISTINGUISHED GUESTS

LT. COLONEL HENRY P. DUNBAR

Mrs. Cushing, Governor Saltonstall, General Miles, General Rankin, Colonel Gillette, Colonel Noyes, distinguished guests, ladies and gentlemen:

We are here to join in the dedication of this General Hospital. It has been an important and interesting task throughout—involving the con-

* Thanks to the generous co-operation of Col. Noyes, the Society is pleased to be able to issue the full dedication proceedings of the Cushing General Hospital. The Society hopes that the Hospital may later bear the more appropriate official designation of the Harvey Cushing General Hospital.

struction of 93 separate units of permanent masonry work, constituting the largest unit under one roof in Massachusetts. The newest practical developments of medical science and engineering skill have been incorporated into the design and construction of this medical center. It has afforded Colonel Gillette and me great satisfaction to know that this task has been commended by the Surgeon General and the Chief of Engineers and has been suggested as a model for others to follow.

This hospital is to be named for Doctor Harvey Cushing in recognition of the great and humane service he rendered during World War I and until his death in 1939.

His Excellency, Leverett Saltonstall, Governor of the Commonwealth of Massachusetts, has followed the construction of this hospital and has visited it on several occasions during construction, having a natural interest in this most valuable addition to the excellent medical facilities already existing in the Commonwealth.

I am privileged to present His Excellency, the Governor of Massachusetts.

GREETINGS OF THE COMMONWEALTH OF MASSACHUSETTS

His Excellency Leverett Saltonstall

Governor Saltonstall extended greetings from the Commonwealth and said:

"It is natural that in this State we should have a hospital concentrated on neurosurgery because of the great work Dr. Cushing did in that field here. The Commonwealth is proud that we have this great Hospital in our midst. We have seen the Hospital grow from the ground in eight months' time and in spite of the almost phenomenal rapidity of its construction, the great medical center is sturdily built."

In conclusion he congratulated all who had a part in its establishment and promised the co-operation of the Commonwealth in every possible way.

Colonel Dunbar: *The Cushing General Hospital will be under the jurisdiction of Major General Sherman Miles, Commanding General of the First Service Command. General Miles was active in the planning of this Hospital and has followed the progress of the work with his usual keen interest.*

I have the honor to present to you General Miles.

ADDRESS

Major General Sherman Miles

The First Service Command is proud to include the Cushing General Hospital among its installations. It will memorialize a great soldier, a great surgeon, and a great gentleman. Harvey Cushing was all of these and more. Military men admired him because he exemplified all that is noble in the

service. He insisted on seeing the First World War from the front lines, activated not by any quest for glory, but by his desire to fulfill his Hippocratic oath with complete disregard for his own safety and comfort.

He served with a Harvard ambulance unit in France in 1915 before the United States entered the war. Realizing that American participation was inevitable, he returned to this country and organized base hospital units as part of the general preparedness campaign. He sailed back to France in 1917 as director of Base Hospital No. 5, the second unit which our Army sent overseas. After his arrival in Europe he undertook a hundred different duties, adapting himself to a program that scorned the calendar and the clock. The major engagements at Château Thierry, St. Mihiel, and the Argonne claimed his presence and his almost miraculous surgical skill; so did the medical councils of Paris and London. His domain was boundless, stretching from front lines to base hospitals and touching *postes de secours*, ambulance trains, and casualty clearing stations.

A grateful government is paying part of its debt to this great man by providing a permanent memorial in the utilitarian form Dr. Cushing would most desire. The beauty and permanence of this structure are secondary to its purpose—ministration to the sick and wounded. The glory of war is transitory, but the horror of war will live in the broken bodies of soldiers who are returned here for treatment.

"For thence—a paradox which comforts while it mocks—shall life succeed in that it seems to fail." Man, on the one hand, girds for war and destruction at tremendous costs; on the other, he provides great havens of mercy for the care of the victims of his wars. He is as determined to save life as to destroy it. Medicine maintains its place in the scientific race, matching each new destruction with a new cure. This hospital we are dedicating today is a model; it has been planned scientifically and equipped with the latest weapons for the war against sickness and suffering and death.

That men should pay for peace with their lives is sometimes inevitable. The Army's sole purpose is to purchase that peace at the least possible cost so far as human lives are the medium of exchange. Victory now appears certain, albeit remote. But the price of victory looms large. This great hospital, like the man for whom it is named, will strive to reduce that price. Every man and woman on its staff will have that end in mind; every man and woman will be dedicated to soothing the wounded, to mending their bodies and their minds, to sending them back into a world grown young and green again.

More than twenty-five years ago, Dr. Cushing sought to mobilize three Red Cross hospitals on Boston Common. He wanted to make people see what must be done to heal the wounds of war. He was frustrated by those who were blind to what he saw so clearly. So he sailed with his own unit for France. And now, in a later war, a grateful Army acknowledges his wisdom and offers to his memory this modern medical center. No memorial could be more fitting to the man. May it always exemplify his high ideals.

COLONEL DUNBAR: *It is fitting that the Cushing General Hospital be officially turned over to the Medical Department by Colonel George W. Gillette, New England Division Engineer. It was under his direction and guidance that the project was planned and completed. His satisfaction with the result attained will always be a source of gratification to me and to all other members of the Boston District organization who participated in the work.*

PRESENTATION OF THE HOSPITAL TO THE MEDICAL DEPARTMENT, U. S. ARMY

COLONEL GEORGE W. GILLETTE

It has been a great privilege indeed to be associated with, and to bear some of the responsibility for, the design and erection of this institution of service to humanity. That sense of privilege is enhanced by the fact that it will bear the name of Dr. Harvey Cushing, a great doctor, a great humanitarian, a great scientist, and a great soldier too.

It is with understandable pride that the people of this great Commonwealth think of Dr. Cushing as their very own; for most of his professional life was spent here and his great reputation and contribution to the world of medicine and science and humanity were made here. But their claims will be disputed by the rest of the country and indeed, by much of the rest of the world. For his was a universal kind of greatness that caused him to be claimed by every human being everywhere. And his kind of contribution was such that it is not limited by considerations of time but belongs to the ages. New techniques and ideas were developed by him which will for centuries to come serve as a foundation for the structure of continuing progress in the delicate and difficult field of medicine to which he devoted his life and genius.

This fine hospital will be a fitting monument to him. It will carry on the great work of healing and research which he began so many years ago. And it will minister, too, to the wounds and hurts of war-torn bodies and minds in much the same way that he did during the First World War. In that time, Dr. Cushing went to help the wounded on the field of battle. In this time, however, the wounded will be brought from the battlefield to this hospital bearing his name. The spirit of his accomplishments was an inspiration to the Engineers in the quality of their work during the construction. His accomplishments will inspire the kind and quality of work that will be done here in the future.

We have tried to make this hospital the best that careful planning and workmanship could make it, in line with the tradition of the Corps of Engineers. We hope we have succeeded. For whatever measure of success that was attained I should like to express my sincere appreciation to Colonel Noyes and Colonel Isherwood of the Army Medical Corps for their co-operation, and to the District Engineer, and his staff; the architects (Stevens,

Curtin, Mason & Riley); Mr. William H. Nye, Vice-President of Turner Construction Company, and his staff; and the other contractors, all of whom have contributed so much by their co-operation to the final result which you see here today.

Let us all hope that those who enter here as patients will leave fully healed under the benevolent inspiration of the great man after whom this hospital has been named, the fine ministrations of Colonel Noyes and his staff, and the complete physical facilities that so many of us have helped to build together.

And now, General Rankin, it is with pleasure and pride that the Corps of Engineers turns over to the Medical Corps the Cushing General Hospital. May it serve humanity well and glorify the United States Army.

ACCEPTANCE OF THE HOSPITAL AND PRESENTATION TO THE COMMANDING OFFICER

BRIGADIER GENERAL FRED W. RANKIN

It is a pleasant task for me to represent the Surgeon General of the U. S. Army at these ceremonies to dedicate the physical plant of a military hospital named in honor of one of the giants of surgery, Dr. Harvey Cushing. This installation now becomes another unit of our Army designed to fulfill a vital mission in support of our assembled military might.

Warfare is usually the result of an effort to impose by force the collective will and beliefs of a people on others and to obtain and establish dominion over them. The designs and character of our present-day conquest-minded enemies have long been apparent to many and, since their initial treacherous attack upon us, should be apparent to all. Our purpose in this life-and-death struggle is, therefore, crystal clear; we fight to resist enslavement and to assure our freedom and dignity. In order to achieve these objectives, we must, by combat superiority, completely destroy the fighting forces hostile to us. This is an immense task but one that we must and can do although it requires the vigorous, unflagging efforts and the unflinching determination of us all.

The successful prosecution of war consists largely of a combination of superior logistics and firepower. The former term connotes a more prosaic and less spectacular function but one that is equally important in waging war effectively since it is concerned with collecting, transporting and delivering the munitions and all other essentials of combat. In this category of supply service lies the function of the Medical Department. Its rôle is vital to the efficient operation of a military machine, for a sick soldier cannot fight, and an unhealthy army cannot do strong battle. We are charged with the conservation and maintenance of health conditions which will not only preserve but also enhance the physical endurance and mental powers of fighting men at the peak level required to assure strategic, tactical, and com-

bat superiority. The number of soldiers we can keep firing guns and the number of sick and wounded we return to the fighting ranks is a measure of our efficiency. We are, therefore, intimately concerned with the soldier's health and all the factors that affect it, from the time he enters the Army until the day he leaves. The importance and magnitude of these responsibilities are reflected by the tremendous expansion of our medical-officer personnel which, by withdrawing approximately forty per cent of the usable physicians of this country, has strained the professional resources of the nation. We are providing our soldiers with a chain of medical care that extends through every echelon of service from the front line of battle to the general hospitals here at home. Representing the final link in this chain the general hospitals typify the ultimate in medical science and technical skill. Completely equipped with the most modern facilities and staffed with the most talented men of the profession, these hospitals are designed to provide the final phases of definitive medical and surgical care. Their highly important mission is concerned with the physical and mental rehabilitation of war casualties. The skilful reconstructive surgery and the expert psychological reconditioning that are instituted here will permit the salvage of the maximum number of these casualties and allow them to resume a happier and more useful place in industry and society. There are now forty-eight of these general hospitals in operation and provisions for eleven more have been made. A certain number of them have been designated as specialized centers for the treatment of conditions requiring a high degree of specialization and proficiency, such as surgery of the chest, vascular system, central nervous system and others.

This hospital named for the master neurological surgeon should be the capstone of the neurosurgical art as practiced in our Army. A memorial to his epochal contributions to medical science, both in war and in peace, it should serve to inspire to higher efforts all who have the privilege of working here.

Dr. Harvey Cushing lives in the hearts and minds of the present medical generation as a scientific investigator, a master surgeon, an inspiring teacher, a gallant soldier and a medical historian, celebrated throughout the world for his prolific investigations in the fields of physiology, pathology, and surgery of the central nervous system, for his originality of thought, and for the profound scope of his activities. Only those of us who were privileged to know him can fully appreciate the sterling qualities and the unique genius of this really great man. He was inately endowed with a grand heritage and many of his attributes and characteristics—for example, his untiring energy, his indomitable resoluteness, his apparent austerity and his pungent forthrightness—reflect his Puritan stock and New England background. These attributes and characteristics, enhanced by brilliant environment and the careful tutelage of that illustrious surgeon, William Stewart Halsted, laid the foundation for his subsequent development and success. Of all of Halsted's eminent pupils, none was more receptive of his teachings, or acquired

more thoroughly his concepts of the art of surgery. The importance of the meticulous and gentle technique which keynoted the mechanistic aspects of surgery in Halsted's clinic was quickly appreciated by Cushing. In this he recognized a new approach to further the boundaries of surgery and it undoubtedly played a major factor in permitting him to open and develop the field of neurosurgery. Introduced to the experimental laboratory, he soon realized that the future progress of clinical surgery was dependent upon a better knowledge of the fundamental chemobiological sciences and a more thorough comprehension of physiological disorders. Along these basic principles, he directed his prodigious efforts in all of his subsequent activities and upon them he built slowly but firmly the foundation of surgery of the central nervous system.

Dr. Cushing's interest in and contributions to military surgery augmented the record of the Medical Department of the U. S. Army in World War No. 1 enormously. With the beginning of that conflict, he turned his interest to the military and devoted his time and energy throughout the whole war to improving the surgical management of the wounded. Both as an active operating surgeon with our own and the British Expeditionary Forces, he contributed his mature experience to the end that intracranial injuries were handled expeditiously and with a hugely lessened mortality. It is safe to say that his invaluable knowledge and recognized capabilities in this field, which led to his appointment as chief consultant in Neurosurgery in the American Expeditionary Forces, evolved methods for the surgical care of these wounds, the soundness of which is shown by the fact that they are today utilized by all Armies engaged in the present global struggle.

It is not permitted me to give here even a brief account of Dr. Cushing's accomplishments and contributions to the sum total of medical knowledge nor to review the honors bestowed upon him by his own and foreign countries. That will be the happy assignment of his biographer, but as his sincere admirer I may emphasize that here was a man, inherently endowed with a remarkable versatility, with untiring industry, with a never-ending reserve of energy, with a keenly analytical and restless mentality, and with a rigid attitude of perfectionism, who was able during his life-span to embrace a wide scope of activities and to attain seemingly unscalable heights in all his endeavors. It is difficult, indeed impossible, to measure his greatness in terms of these invaluable achievements. His eminence transcends materialistic contributions. He belongs to that small but immortal group who pause briefly through the ages to give new meaning to life, to create new institutions for the betterment of mankind, and to leave to posterity an example which serves as a constant stimulus and source of inspiration.

This hospital which I now accept from the Engineering Corps, in the name of the Surgeon General, will, I am convinced, under the direction of its capable Commanding Officer and his staff, live up to the name it bears and add greater lustre to the record of the Medical Department of the United States Army.

ACCEPTANCE OF THE HOSPITAL

COLONEL EDWARD A. NOYES

I believe that it is the ambition of every medical officer, at least of one who has made the Army his life work, to command a general hospital at some time during his career. After the United States entered this war and general hospitals began to spring up in every section of the country I began to wonder, at times, if I should ever realize that ambition. When I was ordered here in October, in time to see the hospital taking on its final form, I soon realized that I had been signally honored by the Surgeon General in being selected to command the Cushing General Hospital.

During last November I had an opportunity to visit and inspect most of the recently constructed general hospitals located in the Southern States. When I returned to this hospital, it was with the firm conviction that the Cushing General Hospital had many advantages over those that I had seen.

In assuming command of this hospital I appreciate fully that with the honor there goes a grave responsibility, a responsibility to the Surgeon General, to merit his confidence in my assignment, and a responsibility for the functioning of this hospital in a manner that will, at all times, do honor to the name it so proudly bears. To that end I pledge the full energy and effort of myself and my staff.

COLONEL DUNBAR: *We are singularly fortunate in having with us Dr. John F. Fulton of the Yale University School of Medicine, distinguished physician, author, teacher, long an intimate associate of Dr. Cushing, presently engaged in writing Dr. Cushing's biography.*

Surely no more appropriate person could be found to dedicate this hospital to Dr. Cushing's memory.

DEDICATORY ADDRESS

DR. JOHN F. FULTON

Some years ago, Dr. Cushing gave an address entitled *The Personality of a Hospital.*[1] The occasion was the centennial of a sister institution of this state, the Massachusetts General Hospital—the "M.G.H."—but the remarks made then apply quite as well now. "Many of us," he said, "have known hospitals under perishable and tattered canvas which possessed an individuality, character and spirit often found lacking in others encased in a more enduring shell of brick and mortar. . . . So it is not the externals nor the inherited wealth, social position or occupation of an institution, any more than of an individual, which give it renown,—it is the character of the service it performs."

---

[1] Cushing, Harvey, The Personality of a Hospital. Ether Day Address—Massachusetts General Hospital. October 18, 1921. *Boston med. surg. J.*, Nov. 3, 1921, *185:* 529–536. (Reprinted in book form, Boston, 1930, 40 pp.)

The reference to perishable and tattered canvas stems from a wide knowledge of military hospitals and surgery, for Dr. Cushing had come from a long line of physicians, many of whom at one time or another had served in the armed forces. Matthew Cushing, his ancestor, had come to this country from England in 1638. Matthew begat John, from John came Matthew the 2nd; then Josiah who was followed by the two Davids, and Dr. David Cushing, Jr., physician of Rehoboth, Massachusetts, and father of Erastus, saw apprentice service during the American Revolution. Erastus, aged 10 during the War of 1812, found himself in Cleveland in 1835 as physician and head of a flourishing family. Henry Kirke, his eldest son, the father of Harvey, acted as chief surgeon to the 7th Regiment of Ohio Militia and was on active duty with the Northern Armies for four years; he cared for the wounded in many major battles including Gettysburg.

With this vigorous American background it was little wonder that Harvey, the tenth and youngest child of Henry Kirke Cushing by his wife, Betsey Williams, should have plunged into war activity once opportunity presented itself. Although much disappointed in 1899 because Dr. Simon Flexner had not taken him to the Philippines, early in 1915, as you are aware from the moving tributes of General Miles and General Rankin, Cushing organized a Harvard Unit and promptly took it abroad to serve with the American Hospital in Paris. In May 1917 after the United States had come into the war, he was appointed Director of Army Base Hospital No. 5 which served in France for nearly two years.

Dr. Cushing proved a dynamic force wherever he moved. His temperament, at times stormy, was also capable of infinite patience, but when he wished something done he was a man of persistence and unyielding determination. As a soldier from civil life he retained a quaint disregard for authority and he never quite accustomed himself to the use of military "channels," but despite this he managed to emerge without being court-martialed, nor yet was he made Surgeon General; both contingencies, however, were at one time within the realm of possibility.

I cannot describe Dr. Cushing's many contributions to medicine and surgery. He did much to extend our understanding of wartime injuries of the head—cranial wound ballistics, as we now define them. He also proved that if a man has energy, curiosity and a driving desire to help the wounded, it is possible, even when under fire, to make scientific contributions of the first water. As with Vesalius, Ambroise Paré, and Weir Mitchell, war became a stimulus rather than a deterrent to positive achievement. One has only to enumerate his introduction of the use of suction in neurosurgical procedures, his employment of the magnet for withdrawing deeply embedded shell fragments, the silver clip for hemostasis, not to mention a host of other less dramatic procedures which together served to convert wartime surgery of the head from a horror into one of the most fruitful and gratifying of all branches of traumatic surgery.

Constantly striving for improved methods of hemostasis, he was led,

some years after the last war, to introduce electrosurgical methods for ablation of vascular tumors; and today the coagulating- and cutting-current units are standard equipment in every large civilian and military American operating room. How fascinated and gratified Dr. Cushing would have been could he have known that his pupils in this war, following in his tradition, have similarly been inspired to positive achievement. Eagerly would he have read Hugh Cairns and Howard Florey's epic report[2] on the use of penicillin in the campaign in Sicily, particularly as it was applied in dealing with head injuries; and, more recently, he would have heartily welcomed the discovery of Franc Ingraham and Orville Bailey[3] that fibrin foam, a bi-product of Edwin Cohn's masterly separation of the various blood proteins for purposes of transfusion, can be used with dramatic effectiveness as a hemostatic agent both in neurological and general surgery, and also in dental surgery. A war that brings such things to the fore cannot have been fought wholly in vain.

The personnel of our Armed Services has gone forward in this spirit, and the subtle influence which Harvey Cushing exerted upon the whole medical profession finds expression today in the atmosphere and personality which you, Sir, [turning to Colonel Noyes] have already made so evident in this hospital. Completed nine months after it was first started, the Cushing General Hospital has already taken upon itself qualities distinctly human, not only in matters of time sequence, but in the spirit and achievements of its staff. The turbulent prenatal period of the institution was presided over by men who had a burning pride in their work. Indeed it would seem that Colonel Gillette and his colleagues of the Turner Construction Company wished to outdo Mother Nature and to have their brain-child precipitated, as it were, into Colonel Noyes' lap before he or his staff were ready for the delivery. The engineers and contractors who have performed this remarkable feat have shown the world that we in medicine are perhaps too conventional in our thinking—too hemmed in by our own biological concepts. From them we gain a new and vigorous point of view, which has characterized this and much else they have achieved in this war.

It is perhaps not known to many of you that Harvey Cushing, the surgeon, had once considered becoming an architect. From early childhood he had shown remarkable talents as a draughtsman, and during his years at Yale College his closest friend was Grosvenor Atterbury, the well-known architect who, exactly fifty years later, built at Yale the handsome Medical Library which now houses Dr. Cushing's great collections. Few therefore could have appreciated more than Cushing the miracle that has been

[2] Florey, H. W., and Cairns, Hugh (Brigadier, R.A.M.C.). Investigation of war wounds. Penicillin. A preliminary report to the War Office and the Medical Research Council on investigations concerning the use of penicillin in war wounds. [London] War Office (A.M.D. 7). October, 1943. 114 pp. [Not yet available for general distribution.]

[3] Ingraham, Franc, and Bailey, Orville T. The use of products prepared from human fibrinogen and human thrombin in neurosurgery. Fibrin foams as hemostatic agents; fibrin films in repair of dural defects and in prevention of meningocerebral adhesions. *J. Neurosurg.*, 1944, *1:* 23-39.

wrought in erecting buildings of this size and quality in the brief interval necessitated by an urgent military time-table; and in the light of Dr. Cushing's own wartime experience as a surgeon,—for he knew well hospitals of "perishable and tattered canvas," as well as those having a "more enduring shell of brick and mortar"—he would have appreciated particularly the dignified spirit of co-operation and service which Colonel Noyes has instilled into his entire staff, the hall-mark that gives to a hospital its individuality.

In coming here today, I have wished to set down something characteristic of Dr. Cushing himself. What would he have said or done in dedicating a hospital named for one of his former teachers? He would have inspected the operating rooms and the wards; he would have scrutinized the case histories, and no doubt would have made some lively comment on the record forms—his chief *bête noire* in the last war. Having explored these things, he would perhaps then have looked about for a library, for men cannot do effective work in any profession without access to books. Since Cushing himself was a voluminous writer, and since this hospital is to bear his name, I am authorized to carry the greetings of Yale University, Dr. Cushing's alma mater, and also to present to your Hospital as a gift from the University through its Medical Library, a collection of Dr. Cushing's published writings, including reprints of his papers, the originals of his many surgical monographs, and his literary essays. An attempt has been made to assemble as complete a collection as possible, and it is hoped that these may form the nucleus of an active Hospital Library.

In closing, I can only congratulate the Surgeons General of the Army, James Magee and his successor, Norman Kirk, and the distinguished men of their command, on thus adding to an already most illustrious record of achievement in this war,—adding to it the Cushing General Hospital of Framingham. I would also congratulate Colonels Gillette and Noyes upon the conspicuous parts that they have played in creating this hospital. In the name of the American medical profession, and particularly of those who were fortunate enough to have been Harvey Cushing's pupils, I wish Colonel Noyes and his staff, health and Godspeed in the days that lie ahead.

A STUDY OF GNOSIS, PRAXIS AND LANGUAGE FOLLOWING SECTION OF THE CORPUS CALLOSUM AND ANTERIOR COMMISSURE*

LT. COMDR. ANDREW J. AKELAITIS, MC-V(S), U.S.N.R.

Department of Medicine, Division of Psychiatry, University of Rochester School of Medicine and Dentistry, and the Clinics of the Strong Memorial and Rochester Municipal Hospitals, Rochester, New York

(Received for publication January 3, 1944)

IN A SERIES of papers on the corpus callosum[2,5,6,10,11] evidence has been presented that commissural systems other than the corpus callosum probably play a large rôle in activities that require the coordination of the two hemispheres. In such unilateral activities as writing with the subordinate hand, the recognition of written symbols and wooden letters in the subordinate side[5] and possibly also of letters in the subordinate homonymous field[2,5] after complete section of the corpus callosum points strongly to the presence of subcallosal commissural systems between the dominant and subordinate hemispheres. The anterior commissure is, next to the corpus callosum, apparently, the most important interhemispheral commissural system.

The present paper is concerned with a detailed study of the higher integrative activities of two patients, one with section of the anterior commissure one year after complete section of the corpus callosum, and the other with simultaneous section of the anterior commissure and the anterior half of the corpus callosum. The essential problem consists of an evaluation of the rôle of the anterior commissure in interhemispheral connection after partial or complete section of the corpus callosum.

METHODS OF INVESTIGATION

Since the various tests have been described in detail elsewhere, only a brief résumé will be given. Laterality, including handedness, footedness, and eyedness, was studied by the method described by Smith and Akelaitis.[10] The study of the higher visual functions in each homonymous field included absolute and relative orientation, absolute and relative discrimination of size, and the recognition of color, objects and letters.[2] Praxis was studied in detail.[6] Auditory gnosis included the study of sound localization, the recognition of familiar sounds and the appreciation of music.[4] Tactile gnosia included detailed study of the sensory system (tactile, pain, temperature, position, vibration, localization, deep pressure, two-point discrimination, weight discrimination, appreciation of shape, size, texture and consistency)

* This study was aided by grants furnished by the Ernest L. Woodward Fund and the John and Mary R. Markle Foundation.

The opinions contained in this paper are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

and stereognosis. Temporal-spatial gnosis was studied.[4] Language functions were studied unilaterally and included the receptive aspects, such as visual and tactile lexia, and the expressive aspects, such as graphia.[5]

CASE REPORTS

Case 1 (Hospital Unit #131559). G.E., a white married farmer, aged 35, was admitted to the Strong Memorial Hospital May 2, 1940 and April 19, 1941.

Personal History. As a child he stuttered; this disappeared in adolescence. At 14 he had poliomyelitis which left him with a residual weakness of the right leg. In 1933, at the age of 28, an osteomyelitis of the right tibia and lower femur developed, necessitating a mid-thigh amputation in 1938.

Present Illness. In August 1937 he began to have convulsions associated with a progressive right-sided paralysis and emissive form of aphasia. Dr. W. P. Van Wagenen drained an abscess in the left frontal lobe beneath an osteomyelitis of the skull on September 3, 1937. The hemiplegia cleared up almost completely except for a slight weakness in the right arm. His speech returned but the stutter reappeared and he has noticed occasional difficulty in thinking of the proper word when writing or talking. The grand-mal seizures have continued. They are associated with an aura of "something going to happen" and in the seizure the right arm thrashes about more than the left. Following each generalized seizure he is aphasic for two or three hours and the right arm is paralyzed and feels numb for several hours. Petit-mal attacks occur about once a day.

Physical Status. This was good except for the right mid-thigh amputated stump.

Neurologic Status. Except for an exaggeration of the tendon reflexes in the right arm the examination was negative. Laterality studies revealed right-handedness and right-eyedness. Before amputation he had used his right foot in kicking. Left cerebral dominance was well illustrated by the association of aphasia with a right hemiplegia in 1937.

Special Studies of Praxis, Gnosis and Language Functions. These were normal except for the stutter and a mild emissive form of aphasia. He had difficulty in spelling simple words and when asked to write out the alphabet he was troubled by the letters "t," "u," "v," and "z." He was able to write with either hand (Fig. 1A). When he was aphasic three years ago he had no difficulty understanding what was said to him and what he read. He remembered that he was unable to write with his left hand at that time.

Laboratory Studies. Examination of blood, urine and feces gave normal results. Electroencephalographic studies revealed delta waves in all leads but of greatest amplitude over the left side of the scalp. Ventriculograms disclosed a dilatation of the ventricular system most marked on the left side and a shift of the pineal shadow to the left. These findings suggested cortical atrophy most marked on the left side.

First Operation. On May 17, 1940 a mid-line frontal incision was carried out along the former incision and extended into the right temporal region. The right frontal lobe was easily retracted away from the falx and the corpus callosum was sectioned completely. A scar approximately 2 cm. in diameter was seen over the right superior frontal gyrus (area 8 of Brodmann).

Course. The postoperative course was uneventful. Except for an increased biceps reflex on the right the neurologic status was normal. He had no difficulty using his crutches to walk. The stutter and dysphasia continued unchanged.

On June 5, 1940 a detailed study of praxis, gnosis and language functions was made with findings identical to those found preoperatively. There was no visual agnosia or alexia in either homonymous field, auditory localization in the median plane was intact, stereognosis and tactile lexia remained intact in each hand, and no disturbance of body image was noticed. Study of time-space relationships including the clock test gave normal results. No evidence of dyspraxia was observed at this time or at any time following operation. He was able to write with either hand with eyes open or when blindfolded.

FIG. 1 (Case 1). Specimens of handwriting. *A* before section of the corpus callosum. *B* one year after complete section of the corpus callosum. *C* eighteen months after callosal section and six months after section of the anterior commissure. *B.1* and *C.1* are examples of simultaneously writing with one hand and dealing cards with the other hand. (Reduced $\frac{1}{5}$)

RH, LH—Right hand, left hand. EO, EC—Eyes open, blindfolded. N, D, S—Name, dictated and spontaneous writing.

In March 1941 he fell down a flight of stairs during a seizure, and sustained lacerations of the scalp.

The neurologic status on his second admission showed essentially the same findings as in June 1940 except for slight sensory changes in the right hand. Although modalities such as the tactile, temperature, vibration, two-point discrimination and joint sense were not disturbed, deep pressure sensation was inadequate over the right hand. Weight-discrimination sense was also impaired in this hand. He recognized moderately sized objects in the right hand but could not identify smaller objects such as a shirt-button in this hand. Similarly two-dimensional forms were incorrectly recognized in the right hand. Wooden letters and skin-writing were correctly recognized in the right hand, however. In the clock test he displayed a good deal of awkwardness when the right hand was tested and because of the inability to distinguish between the hour and minute hand he made numerous mistakes in reading and

setting the time. Study of the visual fields was normal. No dyspraxia was observed although dysdiadokokinesis was moderate in the right hand. He was able to write with either hand (Fig. 1B).

Second Operation. On May 19, 1941 the central portion of the old wound was reopened and the anterior commissure cut. The remnants of the septum pellucidum were resected.

Course. The postoperative course was uneventful. The neurologic status remained unchanged for the most part. Two-point discrimination studies revealed a definite disturbance in the right hand, thus: Index finger-tip, right 15 mm., left 6.5 mm.

He was discharged June 26, 1941. He continued to have grand-mal and petit-mal seizures.

He was studied in detail in November 1941 (18 months after callosal section and 6 months after section of the anterior commissure). The general neurological examination disclosed exaggerated reflexes in the right upper extremity, a slight clumsiness in the right hand on the finger-to-nose test with eyes closed and dysdiadokokinesis in the right hand which was more marked when performed with eyes open. By dynamometer, the strength in the right hand was 30 kg. and in the left 25 kg. Careful sensory studies revealed deep pressure, weight discrimination, and the recognition of two-dimensional forms to be disturbed in the right hand. Small objects and wooden letters were misidentified in the right hand but interpretation of skin-writing was intact. The higher visual functions in each homonymous field were not disturbed. Stereoscopic vision was intact. The higher auditory functions, body image and spatial orientation were not impaired. Temporal relationships were intact except for an inability to read and set the hands of the clock correctly with the right hand. He showed no evidence of simultagnosia. No dyspraxia was observed except for a slight clumsiness in the use of the right hand. He was able to write with either hand with eyes open or closed (Fig. 1C). He could write with one hand and deal cards with the other simultaneously.

Case 2 (Hospital Unit #175483). C.P., a depressed, married white woman aged 46, was admitted to the Psychopathic Division of the Rochester Municipal Hospital March 11, 1941.

Family History. One brother, a postal clerk, had had a severe depression similar to that of the patient. After a bilateral prefrontal lobotomy, he became outgoing in his behavior, returned to work and apparently has adjusted well.

Personal History. Physical health has been good. Fourteen years ago, while patient was five-months pregnant, an ovarian cyst was removed. She has one child, a boy of 13.

Personality. She has always been a sensitive, seclusive and worrisome individual. Throughout childhood and adolescence she worried over her family's financial status, over school grades, and many other matters without adequate cause.

Present Illness. In September 1939 the patient began to express ideas of reference and self-condemnation. Her husband was experiencing financial reverses and the patient suspected that people were conspiring against them. She blamed herself for every misfortune to her family and friends. She feared that her son's difficulty in school was a result of the pelvic operation performed while she carried him in utero. In March she attempted suicide by drinking denatured alcohol and was committed to the Buffalo State Hospital in May 1940. She was transferred from there to the Rochester Municipal Hospital. During this ten-months residence she had shown no improvement.

Physical and Neurologic Status. This was normal. She was color blind for red and green. Laterality studies revealed right-handedness, right-footedness and left ocular dominance.

Psychiatric Status. She was a markedly depressed individual with psychomotor retardation and ideas of self-condemnation and futility. Occasionally she showed extreme agitation and expressed ideas of reference. Sensorium, mental capacity and intellect were not impaired.

Special Studies of Praxis, Gnosis and Language Functions. These were normal except for the clock test. She was able, while blindfolded, to read the time and set the hands of the clock to request with the right hand. However, with the left she tended to confuse the hour and minute hand and right and left orientation of the clock hands in 50 per cent of the trials. From memory she drew a plan of her cubicle satisfactorily.

Laboratory Studies. Examination of blood, urine and feces gave normal results. Electro-

encephalograms revealed alpha waves 7–8 per second. An encephalogram taken with the occiput down disclosed a large amount of air over the frontal area. In view of the bilateral prefrontal lobe atrophy Dr. Van Wagenen decided to perform a leucotomy by means of a craniotomy approach.[13] She was transferred to the Strong Memorial Hospital.

Operation. On March 19, 1941 a right fronto-parietal craniotomy was performed and the genu and anterior half of the body of the corpus callosum, the anterior commissure and the right limb of the fornix were sectioned. The septum pellucidum was incised. A bilateral leucotomy was then performed. The atrophy limited to the frontal poles suggested Pick's disease.

Course. The operation was performed under local anesthesia and the patient was studied immediately after closure of the wound. She was a bit drowsy but in good spirits and cooperative. She tired very easily. As complete a psychiatric and neurologic examination as was possible was made for the next two and a half hours while the patient lay on the operating table.

She was disoriented for time, place and person. Her recent memory was much impaired. Remote memory fluctuated; she gave an account of her schooling, marriage and family correctly but said that she had been in the Buffalo State Hospital since 1924. She gave the names of the days of the week and the months, remarked upon the war in which "Japan was fighting all the other countries."

The reflexes were in order. Appreciation of vibration was questionably increased and tactile sensation diminished on the left side. Localization sense was apparently intact. The visual fields were full to rough tests and she recognized objects and letters in either homonymous field. She localized the sound of a vibrating tuning fork in the median plane correctly. Stereognosis was intact in both hands. She recognized skin-writing over the right side adequately but failed to appreciate it over the left side. However, she had no difficulty in recognizing wooden letters in either hand. No difficulty in body-image was found. In the clock test she failed to read the time correctly with either hand and could not be persuaded to make the effort to set the hands of the clock. There was no evidence of dyspraxia in either hand. She was able to remove a paper match from the cover which she held in the opposite hand and strike it afire readily. She did this as easily with the left and right hands as before operation. She was able to write with either hand with eyes open or when blindfolded (Fig. 2A). She correctly held the pad in one hand and the pencil in the other. The accuracy with which she dotted the "i's" and crossed the "t's" while blindfolded was remarkable.

The following day she recognized the examiner but was disoriented for time and place. Although she complained of headache she appeared to be quite happy. The neurologic status remained unchanged. On the third postoperative day she continued confused, was loquacious and seemed to be hallucinated. Her mood would change from elation to depression abruptly. Subsequently she misidentified staff members occasionally, showed a tendency towards punning and rhyming, and her mood was generally one of elation.

She was studied in detail April 10 and 11, 1941 (3 weeks postoperative). The neurologic status was normal. There was no evidence of dyspraxia, dyslexia or dysgraphia in either side (Fig. 2B). Body-image orientation was good and the localization of sound was intact. Temporal gnosis was fairly good, except that, as before operation, she did poorly in the clock test with her left hand. The results of these tests are shown below:

Right Hand		Left Hand	
Clock set at	*Patient reads*	*Clock set at*	*Patient reads*
12:15	12:15	3:30	6:45, 6:15, 11:45
5:45	5:45	9:00	11:45
7:30	7:30	11:15	12:15
Patient requested to set clock at:	*Patient sets hands at:*	*Patient requested to set clock at:*	*Patient sets hands at:*
2:45	2:45	5:45	11:45
8:00	8:00	6:15	12:15
3:30	3:30	8:30	4:00

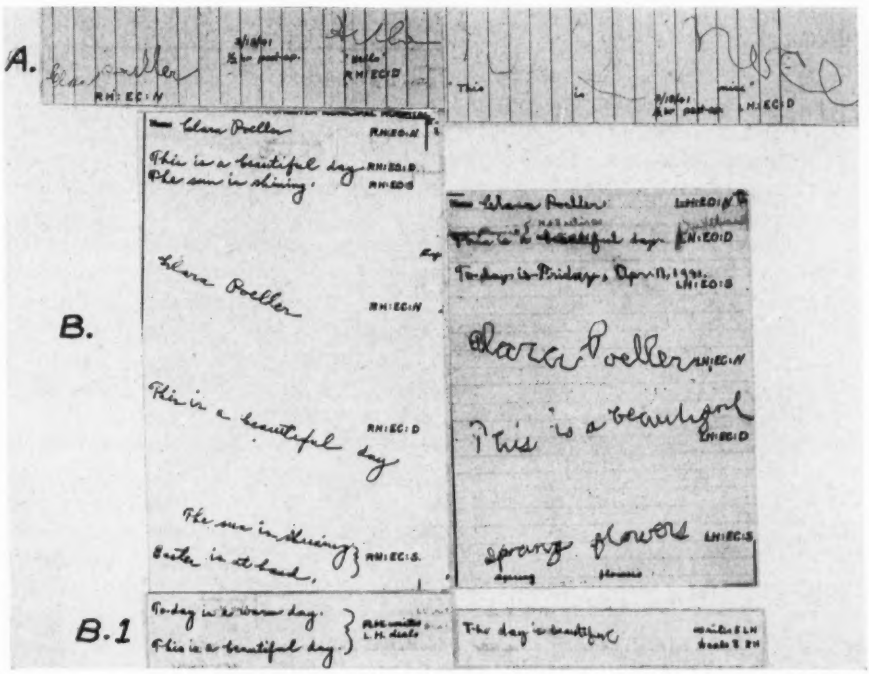


FIG. 2 (Case 2). Specimens of handwriting. *A* one half-hour after and *B* three weeks after operation in which anterior half of corpus callosum, anterior commissure and right fornix were sectioned. *B.1* shows examples of simultaneously writing with one hand and dealing cards with the other hand. (Reduced ½)

Spatial orientation was markedly disturbed. She realized that she was in the Strong Memorial Hospital in Rochester from the conversation of friends, staff-members and the markings on the linen but invariably felt that she was in her home-town, Tonowanda, N. Y. She could draw the plan of her cubicle from memory but confused the relationship of her bed to the other beds. When given a map, she identified the various cities quickly and accurately and traced routes correctly from one city to another. However, if given a piece of paper marked with the points of the compass and with Rochester written in the center she would become hopelessly confused when asked to place other cities in relation to Rochester.

Since discharge home, April 27, 1941, she has remained cheerful, does her housework, has gained in weight, and no apparent difficulty in memory or calculation exists. However, she still feels that she is in some other town than the one she lives in. She admits that she must be wrong but she can never convince herself completely.

DISCUSSION

Case 1 is the more important because there was a complete section of the corpus callosum and of the anterior commissure. It has been suggested by McCulloch and Garol[9] that the apparent contradiction between Erickson's[7] conclusions on experimental convulsions and those cases in which seizures occurred bilaterally after section of the corpus callosum reported by

Van Wagenen and Herren[14] may be explained on the basis of the interhemispheral fibers in the anterior commissure which connect areas 21 bilaterally. Insofar as one can analogize between experimental convulsions and convulsive disorders in humans it becomes apparent that bilateral seizures can recur even after sectioning the corpus callosum and the anterior commissure. These findings complement the results reported in the present paper; namely that interhemispheral neuronic pathways occur at lower levels of the central nervous system.

Following complete section of the corpus callosum no disturbance in visual, auditory and tactile gnosis was observed and praxis and language functions were unimpaired. Similarly, temporal-spatial gnosis (orientation) was intact. Because of changes in the neurologic status, most probably resulting from injury to the brain while in a convulsion ten months following the callosal section, the patient was unable to recognize small objects or two-dimensional forms in the right hand or to do the clock test with this hand. Other functions were unimpaired however. Shortly after the operation in which the anterior commissure was cut the neurologic status continued as before operation except that two-point discrimination sensation was disturbed in the right hand. Six months after section of the anterior commissure the neurologic status had returned to the preoperative condition. It is therefore possible to conclude that gnosis, praxis and language functions are not disturbed in either side following the severance of the interhemispheral fibers in the corpus callosum and the anterior commissure. Although not skilled in finely coordinated bilateral activities, such as piano-playing or typing, the fact that he showed no disturbance in writing with either hand or in interpreting skin-writing on either side strongly suggests the possibility that interhemispheral fibers occurring in commissural pathways other than the anterior commissure and corpus callosum play a prominent part in the connections between the dominant and subordinate hemispheres. There is little doubt regarding the dominance of the left hemisphere for language in this patient because of the previous history of a transient aphasia with the development of a brain abscess in the left frontal lobe.

Case 2 is unique for three reasons. First, in view of the fact that the operation was performed under local anesthesia, it was possible to test gnosis, praxis and language functions immediately after closure of the wound. The fact that no dyspraxia was found in the subordinate hand, that she could write with either hand and recognized wooden letters in the left hand after section of the anterior commissure, right fornix and the anterior half of the corpus callosum disproves completely the possible contention that the subordinate hemisphere quickly relearns the patterns of complex movements and synthesis of complex sensations. Surely, the most probable answer is that other interhemispheral neuron connections can be utilized immediately. The argument can be advanced that after sectioning of the anterior half of the corpus callosum, secondary pathways from the supramarginal and angular gyri of the dominant hemisphere pass through the

splenium to centers in the subordinate hemisphere and thus allow praxis, gnosis and language functions to remain undisturbed in the subordinate side. Unfortunately the callosal section was not complete in Case 2, but the findings in Case 1 prove that these secondary pathways are not essential for the preservation of these functions in the subordinate side.

Second, the interesting state of confusion in spatial relationships which continued for at least six months after operation requires explanation. In a previous paper[4] it was shown that partial or complete section of the corpus callosum results in temporary confusion only if unilateral involvement of the posterior portion of either hemisphere coexists. The moderate bilateral frontal atrophy as disclosed by encephalogram and at operation suggests the possibility that this patient might have Pick's disease. As is generally known, the posterior portions of the cerebrum are infrequently involved in this form of atrophy. Again it should be emphasized that in Case 1 there was no confusion. It seems that this confusion in Case 2 is, in all probability, a result of the bilateral frontal leucotomy. Disturbances in orientation occur very commonly following prefrontal lobotomies (Freeman and Watts,[8] Strecker *et al.*).[12]

Third, the improvement in the emotional status following operation was typical of that observed by others after bilateral prefrontal lobotomy. In other words the additional lesions of the partial callosal section and section of the anterior commissure and right fornix did not modify the therapeutic results. This tends to confirm previous psychobiological studies[1,3] of patients after partial and complete section of the corpus callosum.

SUMMARY AND CONCLUSIONS

The higher integrative activities including praxis, gnosis and language functions were studied unilaterally. In the first patient the anterior commissure was sectioned one year after a complete section of the corpus callosum. In the second patient the anterior commissure, right fornix and the anterior half of the corpus callosum were sectioned under local anesthesia.

In conclusion, evidence has been presented showing that interhemispheral neuronal pathways exist other than those found in the corpus callosum and anterior commissure.

Dr. W. P. Van Wagenen performed the operations on these patients. I wish to express my gratitude to him for his kind cooperation in making his patients available for study.

REFERENCES

1. Akelaitis, A. J. Psychobiological studies following section of the corpus callosum. A preliminary report. *Amer. J. Psychiat.*, 1941, *97:* 1147–1155.
2. Akelaitis, A. J. Studies on the corpus callosum. II. The higher visual functions in each homonymous field following complete section of the corpus callosum. *Arch. Neurol. Psychiat., Chicago*, 1941, *45:* 788–796.
3. Akelaitis, A. J. Studies on the corpus callosum. VIII. The effects of partial and complete section of the corpus callosum on psychopathic epileptics. *Amer. J. Psychiat.*, 1941, *98:* 409–414.
4. Akelaitis, A. J. Studies on the corpus callosum. VI. Orientation (temporal-spatial gnosis) following section of the corpus callosum. *Arch. Neurol. Psychiat., Chicago*, 1942, *48:* 914–937.

5. Akelaitis, A. J. Studies on the corpus callosum. VII. Study of language functions (tactile and visual lexia and graphia) unilaterally following section of the corpus callosum. *J. Neuropath. exp. Neurol.*, 1943, *2:* 226–262.
6. Akelaitis, A. J., Risteen, W. A., Herren, R. Y., and Van Wagenen, W. P. Studies on the corpus callosum. III. A contribution to the study of dyspraxia and apraxia following partial and complete section of the corpus callosum. *Arch. Neurol. Psychiat., Chicago*, 1942, *47:* 971–1007.
7. Erickson, T. C. Spread of the epileptic discharge. An experimental study of the after-discharge induced by electrical stimulation of the cerebral cortex. *Arch. Neurol. Psychiat., Chicago*, 1940, *43:* 429–452.
8. Freeman, W. J., and Watts, J. W. Psychosurgery. Intelligence, emotion and social behavior following prefrontal lobotomy for mental disorders. *Springfield, Ill.: Charles C Thomas*, 1942, 337 pp.
9. McCulloch, W. S., and Garol, H. W. Cortical origin and distribution of corpus callosum and anterior commissure in the monkey (Macaca mulatta). *J. Neurophysiol.*, 1941, *4:* 555–563.
10. Smith, K. U., and Akelaitis, A. J. Studies on the corpus callosum. I. Laterality in behavior and bilateral motor organization in man before and after section of the corpus callosum. *Arch. Neurol. Psychiat., Chicago*, 1942, *47:* 519–543.
11. Smith, K. U., and Akelaitis, A. J. Studies on the corpus callosum. X. Reaction time and speed of motor coordination in man before and after section of the corpus callosum. (To be published)
12. Strecker, E. A., Palmer, H. D., and Grant, F. C. A study of frontal lobotomy. Neurosurgical and psychiatric features and results in 22 cases with a detailed report on 5 chronic schizophrenics. *Amer. J. Psychiat.*, 1942, *98:* 524–532.
13. Van Wagenen, W. P. Personal communication.
14. Van Wagenen, W. P., and Herren, R. Y. Surgical division of commissural pathways in the corpus callosum. Relation to spread of an epileptic attack. *Arch. Neurol. Psychiat., Chicago*, 1940, *44:* 740–759.

THE PHYSIOLOGICAL BASIS OF CONCUSSION*

A. EARL WALKER, M.D., JERRY J. KOLLROS, PH.D. AND THEODORE J. CASE, M.D.

Division of Neurological Surgery and the Otho S. A. Sprague Memorial Institute, the University of Chicago, Chicago, Illinois

(Received for publication January 4, 1944)

INTRODUCTION

CEREBRAL concussion is generally agreed to be a traumatically induced derangement of the nervous system, characterized clinically by temporary impairment of consciousness, dizziness, mild confusion and headache, and unassociated with gross anatomical changes in the brain. In animals Duret[7] described the acute manifestations of concussion as consisting of convulsive and paralytic stages, but clinicians, being impressed by the latter phase, have largely neglected the initial convulsive phenomena. Since Duret's experimental study, technical procedures for precise measurement of intracranial changes have been developed and some understanding of neural mechanisms has been acquired, so that now the phenomena of concussion may be placed upon a sound physiological basis.

METHODS

In all 151 cats, 15 dogs and 21 monkeys have been used in this research. All surgical procedures have been carried out under general anesthesia induced either by inhalation of vinethene (vinyl ether) or nembutal (pentobarbital sodium) given intraperitoneally.

In animals the criteria of concussion are limited, since few objective signs are present. The loss of consciousness, tonic muscular spasm, respiratory and cardiovascular changes, and loss of the corneal reflex are the most constant phenomena. Other clinical manifestations of concussion, so well described by Denny-Brown and Russell,[5] have been observed, but reliance has been placed on the above criteria.

At various times the following methods have been used for producing concussion: (i) Hammer blow to the fixed and the movable head. (ii) Gunshot blow to the head, the bullet passing through an extracranial portion of the head. (iii) A blow delivered by a weight falling through a glass tube upon a column of water in contact with the intact dura mater. Of these methods, which could be made to give identical clinical and physiological results, the last was found to produce the most predictable results, and to cause the least disturbance to apparatus attached to the head.

Early in this study it was found essential to determine the severity of a blow that consistently would produce concussion. This was accomplished by anesthetizing the animal with vinethene (vinyl ether) during the preparation of the head and the injection of one per cent solution of novocaine into the scalp (vinethene-novocaine anesthesia). Tetanic spasm, respiratory and circulatory changes, as well as the reflex alterations were used as criteria of the concussive state. In the cat it was found that a 28 gram weight dropped five feet usually produced concussion. It was assumed that a similar blow would also cause concussion in cats anesthe-

* The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Chicago.

Presented before the American Academy of Neurological Surgery at the Percy Jones General Hospital, Battle Creek, Michigan on September 18, 1943.

tized by other agents, e.g., nembutal. In order to produce a certain concussion in such animals a 50 gram weight was used and rarely failed to cause the respiratory and vascular phenomena characteristic of traumatic unconsciousness.

If accurate measurements of intracranial phenomena were to be made, it was essential that the animal's head be firmly fixed. Since it had been suggested that concussion produced with a fixed head was distinct from that produced with a freely movable head,[5] we examined the clinical phenomena resulting from blows to the fixed and the movable head. With equivalent stimuli we could find no discernible difference in the clinical or physiological sequelae.*

Intracranial pressures were measured from different regions of the head by trephining the calvarium, opening the dura and screwing cannulae into the holes in the skull. The openings of these cannulae were on the side as suggested by Scott,[21] rather than at the end. These cannulae were connected by a water-tight system to Hamilton manometers† which recorded optically on bromide paper. The instruments were frequently calibrated and the accuracy of the responses checked by calculating the pressure produced by a falling weight onto a closed manometric system. Membranes of very short period (less than 1 millisecond), low sensitivity but considerable flexibility were used.

All electrodes were firmly screwed into the bony calvarium to the level of the dura mater. The electrodes were placed in various parts of the head, each pair being 1 to 2 cm. apart (the distance measured each time), but for purposes of recording accurate voltage changes only those on the calvarium opposite to the site of the blow were utilized. We doubt that this precaution is actually necessary—but lest movement of the dura might introduce an artifact it was followed. The amplifiers used for augmenting the E. K. G., E. E. G. and similar potentials were two-sided resistance-capacity-coupled machines with direct coupling between the last two stages, working into an ink-writing oscillograph. For recording the voltage of the electrical discharge immediately following the blow, a potentiometer was connected to the animal so that any fraction of the total voltage could be applied to the amplifier. For recording the form of the electrical discharge a direct coupled amplifier built according to Goodwin's specifications[10] was directly coupled to a two-sided output unit. From this stage it was possible to work either into the ink-writing oscillograph or into a General Electric loop oscillograph.

The time of the blow was recorded by a photoelectric cell, so arranged that at the moment of impact the falling weight interrupted a beam of light focused upon it.‡ The artifacts produced by the falling weight were checked by dropping the weight three times upon the dead cat at the end of the experiment. The first blow after death not infrequently caused a deflection of the ink-writer whereas the latter two blows usually produced little or no deflection.

Blood-pressure recordings were usually made from the carotid artery in the cat, although in the dog and monkey the femoral artery was used. The electrocardiogram was taken from leads to one forelimb and the muscles of the back, or from an Adrian-Bronk needle inserted in the mediastinum.

The brains of all animals were examined. A small subarachnoid hemorrhage at the base of the brain was the most common finding, but in those animals that had sustained only one blow the brain usually appeared normal grossly. We doubt that the subarachnoid hemorrhage present in the brains of these animals played a significant role in the acute phenomena of concussion that are being considered. In a few cats, which had suffered repeated blows, small petechial hemorrhages were found in the brain stem at the level of the mesencephalon. Contrecoup injuries to the hemispheres were occasionally seen but lacerations or primary hemorrhages on the orbital surface of the frontal lobe or tip of the temporal lobe were not seen.

---

* A discussion of the concept of acceleration and compression concussion may be found in the Proceedings of the Association for Research in Nervous and Mental Disease for the meeting held in New York City, December 17, 1943.

† We are indebted to Dr. W. W. Scott who loaned us the Hamilton manometers and instructed us in their use.

‡ We are indebted to Mr. William Funderburk and Mr. Leslie Philips for technical assistance with the electronic equipment.

CLINICAL MANIFESTATIONS OF CONCUSSION

In animals the phenomena associated with cerebral concussion may be analyzed by experimental methods. When so studied each of the clinical manifestations yields valuable evidence as to its pathogenesis.

Tetanic Phenomena. When any animal is struck on the head by a blow of sufficient force to cause immediate unconsciousness, many observers have noted that there is an immediate generalized muscular spasm which Duret[7] has spoken of as the tetanic stage of concussion. Miles[17] has observed tetanic or convulsive phenomena upon cerebral trauma to the rabbit, pig and cock. In the carnivora and the primates such tetanic phenomena are constantly present in varying degrees. Concussion of the cat prepared under vinethene-novocaine anesthesia is frequently associated with a convulsive attack having both tonic and clonic phases and resembling that seen in epileptic seizures induced by electric current or drugs. In the monkey such tonic-clonic fits are less common, usually consisting only of a tonic phase followed by complete muscular relaxation.

These tetanic manifestations of concussion appear to be evidence of intense stimulation of the central nervous system involving not only the lower centers but also the cerebral cortex since the latter appears to be one of the determinants of the clonic phase of a convulsion.[20]

Respiratory Alterations. Although changes in respiration are generally considered to be one of the manifestations of concussion, it is possible by a blow to the head to cause concussion without producing any change in respiration or in circulation.[21] Usually, however, respiratory changes occur with a concussive blow. These may consist of merely a short gasp, with resumption of normal respiration, a gasp with temporary irregular respiration, or a gasp with apnea of short or long duration.

The respiratory alterations resulting from concussion do not resemble the inhibitory respiratory change seen upon stimulation of the cerebral cortex. The former is a spasm of the intercostal and diaphragmatic muscles producing a forced respiratory movement of unusual depth whereas the latter is merely a simple arrest in one phase of respiration. This difference is readily seen if the pneumographic tracings of the respiratory alterations from cerebral stimulation and from cerebral concussion be compared (Fig. 1).

Blood Pressure. An animal may be rendered unconscious by a blow to the head without alteration in the blood pressure or pulse, but usually immediately or within a few seconds after a concussive blow, a rise in blood pressure of varying degree occurs. This arterial hypertension is, like the respiratory arrest, due to the effect of the trauma upon the brain stem, for it may be produced by concussion in the decerebrate animal. Harvey Cushing[3] showed that the rise of blood pressure did not occur if the spinal cord were cut. If a curarized animal (anesthetized) which has previously had both vagus nerves sectioned is subjected to cerebral trauma sufficient to produce the concussive phenomena and within one-half second after the blow the cervical spinal cord be sectioned, the rise in blood pressure will occur as high as in control preparations in which the cord has not been sectioned (Fig. 2). Since

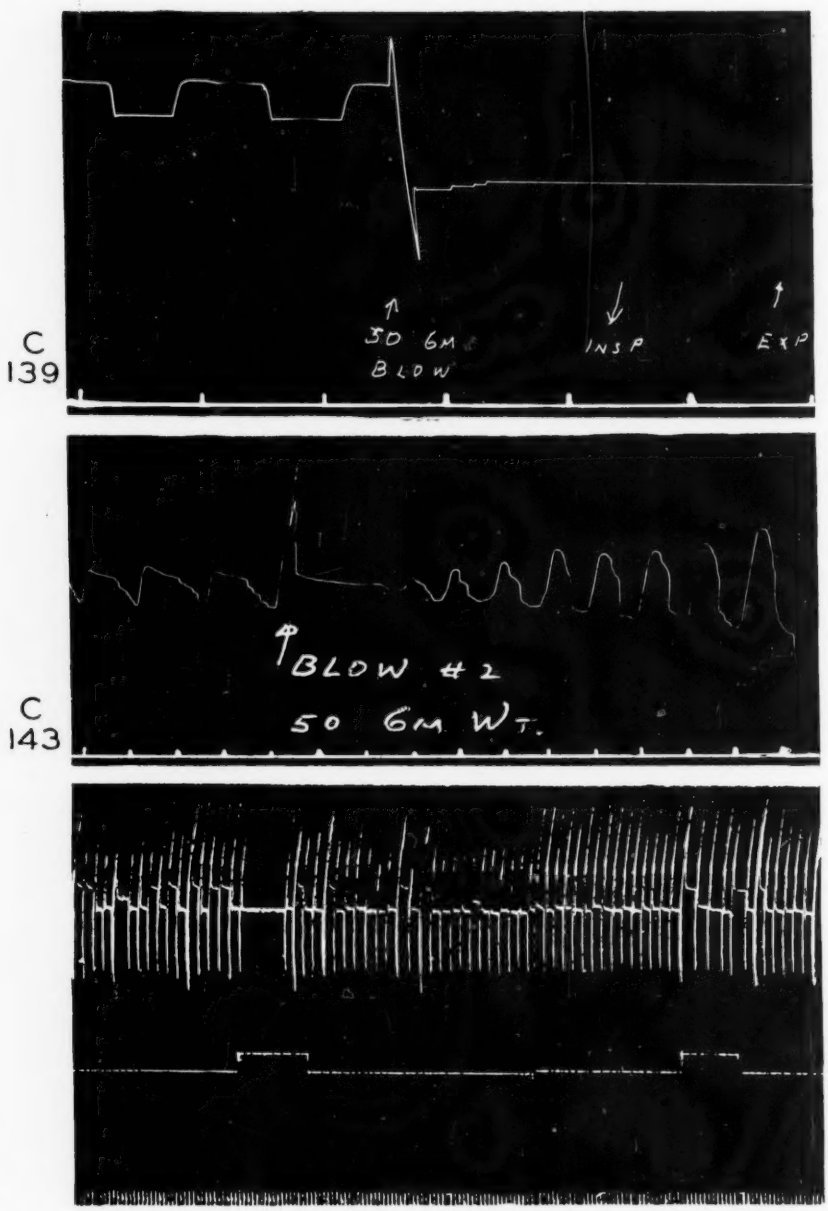


FIG. 1. Pneumograms showing in the upper two records the forced respiratory movements following cerebral concussion in the cat and in the lower record the respiratory arrest induced by electrical excitation of area 6 Bβ in the macaque monkey. The dynamic respiratory effect in the first two records contrasts sharply with the inhibitory apnoea in the third. (Time is indicated in seconds at the bottom of each record.)

simple section of the spinal cord does not produce appreciable arterial hypertension, this observation would indicate that the blow itself caused an intense stimulation of the vasomotor centers leading to peripheral vasoconstriction.

Brachycardia. Not infrequently, at the moment of the blow or within one beat thereafter, a marked slowing of the pulse is noted. This does not occur if the vagus nerves have been sectioned. The pulse may return to its preoperative rate within a few seconds, following which a secondary slowing

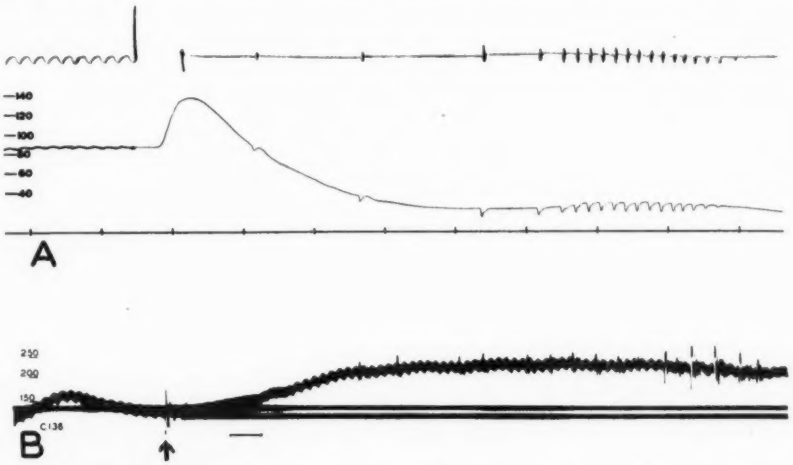


FIG. 2. *A*. Pneumogram (upper tracing) and sphygmogram of a decerebrated cat which was shot with a .22 bullet through the empty calvarium. The respiratory and blood pressure alterations are the same as seen when a normal cat is concussed. (Time is indicated on the base line in 10-second intervals.) *B*. Sphygmogram from the right carotid artery of a curarized cat anesthetized by intraperitoneal nembutal with both vagus nerves sectioned, which was being given artificial respiration. At the arrow, the animal was concussed and one-half second later (at the beginning of the second base line) the spinal cord was transected at the first cervical segment. The blood pressure rise is as high as occurs in concussed animals with intact spinal cords. (A one-second interval is indicated by the short line below the baseline.)

usually occurs. The primary immediate slowing of the pulse appears to be due to vagus excitation as the result of the blow itself (Fig. 3).

Reflex Changes. In the spinal cord, immediately after a concussive blow, the tendon reflexes may be abolished and the threshold of the anterior horn cells heightened. If the spinal cord is sectioned before the blow is delivered, there is no alteration in the tendon reflexes, nor is there a change in the threshold of the anterior horn cells to electrical excitation. These observations suggest that the effect on the reflex arc is not a mechanical one due to the blow, but a physiological alteration secondary to the effect of the blow on cerebral structures.

These experimental observations of clinical phenomena present evidence that at the moment of a concussive blow, intense stimulation of the cerebral

cortex and the brain stem occur producing physiological responses characteristic of excitation. None of these changes is secondary to alterations in the circulation, oxygenation, metabolism or acid-base regulation of the cerebral cortex since they occur within a fraction of a second and before such alterations can take place.

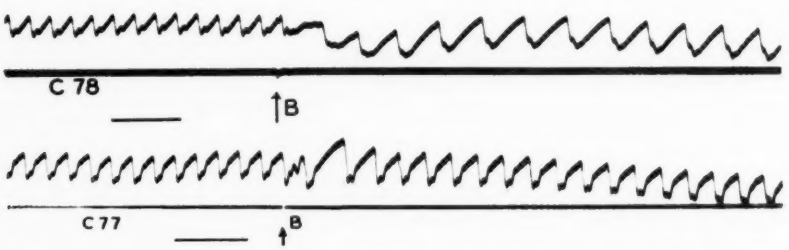


FIG. 3. Sphygmograms taken from the carotid arteries of two cats showing the marked slowing of the heart occurring within one systole of a concussive blow (indicated by the arrows). (A one-second interval is indicated by the line to the left of the arrow.)

ELECTRICAL DISTURBANCES DURING CONCUSSION

With the impact of a blow on the head, marked changes in the electrical potentials occur within the central nervous system. This phenomenon, although present in the records of previous experimenters,[25] appears to have been considered the result of the blow upon the calvarium and not due to intrinsic biological changes in the central nervous system. However, in a curarized (anesthetized) animal receiving artificial respiration with proper amplification and the use of a voltage divider so that rather large potentials may be measured without blocking the amplifier, it may be shown that at the moment of impact potentials from a few hundred microvolts to a millivolt or more may be picked up from the cerebral cortex, while in the dead animal deflections are equivalent to a discharge of from only ten to a few hundred microvolts at the most. These potential discharges are not entirely predictable, varying from preparation to preparation with the severity of the blow and with the location of the electrodes (Fig. 5).

The discharge is probably larger near the site of the blow, but since our experimental technique may not allow the same physical state at the site of the blow as at other parts of the brain (movement of the dura is a possible but unlikely source of artifact at the site of the blow which cannot be controlled) we cannot state this with certainty. If a blow is struck in one parietal region in the monkey, the greatest discharge on the opposite side is from the motor region, the next largest from the parietal region, and the least from the frontal and occipital poles. Electrodes across the brain stem (one in the sphenoid bone just posterior to the pituitary fossa and the other in the midline of the occipital bone just above the foramen magnum) reveal a discharge slightly greater than that obtained from the parietal region. However, it

must be remembered that the absolute potential change is of little significance, since factors such as position of electrodes, severity of blow, condition of the animal, etc. cannot be accurately controlled. With repeated blows at intervals of less than four hours, the cortical potential discharge tends to decrease and may be quite small at the final fatal blow.

In the vinethene-novocaine anesthetized and curarized (anesthetized) animal, following the initial discharge, there occurs a marked increase in the frequency of the cortical activity with little decrease in amplitude. This fast

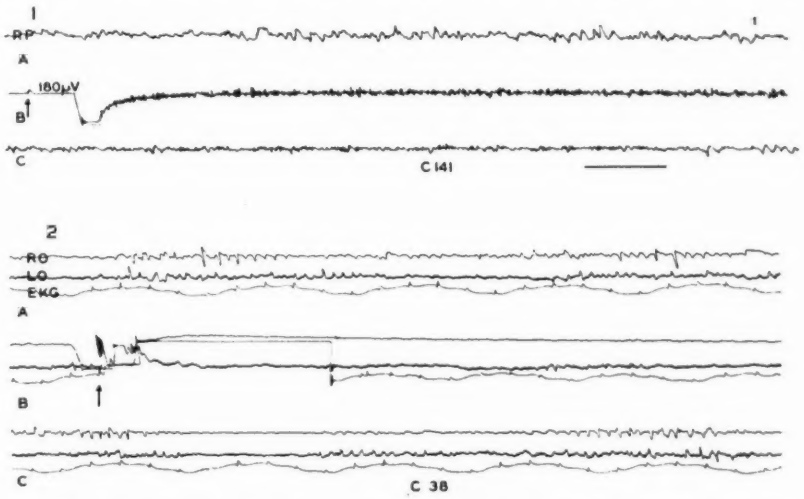


FIG. 4. Electroencephalograms of two cats. *1.* Anesthetized by vinethene and novocaine, curarized and artificially ventilated. *2.* Anesthetized by intraperitoneal nembutal. Each cat was concussed at the arrow. In the first cat there is increase in the frequency of the cortical activity, but in the second animal there is an immediate decrease in all activity. Following the immediate increased activity of the cortex of the first animal, the electrical activity decreased (*1-C*). In both animals the activity returned to normal after a few minutes. The abbreviations used are as follows: RP, right parietal leads; RO, right occipital leads; LO, left occipital leads; EKG, Adrian-Bronk needle in mediastinum. (A one-second interval is indicated by the line below the first series of records.)

spiky cortical activity is not unlike that seen during a major convulsive seizure, and in fact it may be so accompanied in a non-curarized animal. Nembutal anesthesia obscures this afterdischarge as well as its clinical concomitant, the tonic-clonic muscular response. This increased activity persists usually for 10 to 20 seconds and then gradually decreases so that the cortex becomes relatively inactive for a period of a few seconds to minutes following which the electrical activity slowly regains its normal level (Fig. 4).

The increased activity following the initial discharge must be considered an afterdischarge or long-lasting facilitation (Lorente de Nó[15]) occasioned by the passage of impulses through internuncial chains—"re-

verberating circuits" (Ranson and Hinsey[19]). Associated with this facilitation is, according to Dusser de Barenne and McCulloch,[8] an increase of subliminal stimulation leading to summation, negative voltage drifts associated with a decrease of threshold in neurons previously discharged, and an increase of pH, which decreases the threshold of all neural structures involved. Two of these factors we have been able to demonstrate as present in the afterdischarge following cerebral concussion. One might conclude that the tonic-clonic fit is in itself evidence of a decreased threshold of the cortical neurons, but we have been able also on occasion to demonstrate a

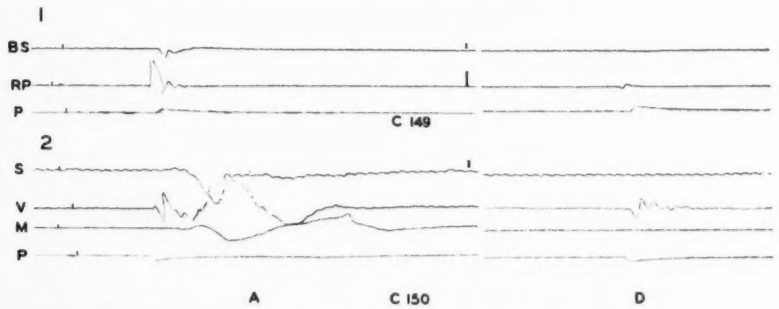


FIG. 5. *1.* Potentials from the brain stem (BS—one lead in the midline of the sphenoid bone near the pituitary fossa and the other in the midline of the occipital bone just above the foramen magnum) and right parietal region (RP) as the result of a blow in the left parietal region indicated by the photoelectric cell (P). The cat was anesthetized, curarized and artificially aerated. The alignment of the pens is shown at the left and the vertical lines at the right of the first tracing represent a deflection of 500 μV in each amplifier. At the right is the artifact produced by a blow in the left parietal region of the dead cat. *2.* Potentials from the sciatic (S), vago-sympathetic trunk (V), and median (M) nerves of an anesthetized, curarized, artificially aerated cat, resulting from a concussive blow indicated by the photoelectric cell (P). The alignment of the pens is shown at the left. The vertical line at the right of the first tracing represents a deflection of 60 μV. Note the double diphasic wave in the vagosympathetic tracing, the second portion of which probably represents excitation of the sympathetic fibers which are associated with the vagus nerve in the cat. A 60 cycle per second sine wave has been superimposed upon the sciatic tracing to act as a time record. The record to the right (D) was obtained by concussing the dead cat, other conditions remaining as previously.

decreased threshold to electrical excitation of the motor cortex in this period of afterdischarge. We have also shown by direct coupled amplifiers that there is a sharp negative voltage drift at the moment of the concussion in the motor area and that the cortex remains negative for several seconds afterwards with respect to the posterior parietal region.

Following this afterdischarge is a period of decreased spontaneous electrical activity of the cerebral cortex which physiologically is "extinction." Dusser de Barenne and McCulloch[8] conclude that this phenomenon is associated with diminished subliminal excitation resulting in less summation, positive voltage drifts with increase of thresholds of neurons previously discharged, and a decrease in pH. The electroencephalographic picture of decreased cortical activity is evidence of diminished subliminal excitation. We

have demonstrated after concussive blows that following the period of electrical negativity there is a positive drift, and an increase in the threshold of the motor cortex.

It therefore appears that the electrical phenomena following concussion may be well explained by the known characteristics of neuronal excitation.

Electrical Disturbances in Peripheral Nerves. In a curarized and anesthetized animal being artificially ventilated, electrodes placed upon the phrenic, vagus, sciatic, median or supraclavicular nerves and connected to suitable amplifiers reveal a large electrical discharge shortly after cerebral concussion. If an Adrian-Bronk needle is placed within the spinal cord a similar discharge may be found immediately following the concussive blow, which does not occur if the spinal cord has been transected or in the dead animal (Fig. 5). These experimental demonstrations indicate that there is at the moment of the blow a marked electrical discharge within the central nervous system which affects all parts of the nervous system to varying degrees and which manifests itself by excitation of the peripheral nerves.

MECHANISM OF THE EXCITATION

It is obvious that the electrical potentials developing at the time of concussion must be derived from polarized structures within the central nervous system. At least two such polarized systems are present. One is the axone whose surrounding sheath maintains a polarized condition except during actual passage of the nerve impulse, the other is the nerve cell whose membrane appears to act as a polarized surface and against which lie the end processes of many axones which are likewise bioelectrically charged. Of these two systems, it seems most likely that it is the cell membrane of the neuron which gives rise to the phenomena. Krems, Schoepfle and Erlanger[14] found that an air blast applied to an exposed nerve may elicit a maximal twitch of the muscle due to mechanical stimulation of the nerve. Subsequent test shocks reveal a marked reduction of the muscle response for 3 to 5 minutes and occasionally ten minutes. The axones of the central nervous system might similarly respond to trauma, but if so, their recovery is quite rapid, much more so than that of the neuron. It therefore seems likely that the electrical discharge at the moment of concussion is the result of depolarizing many cells within the central nervous system. This electrical breakdown of the cell membranes fires the axones producing widespread excitation both centrally and peripherally.

The physical mechanism by which the polarized membrane of the cell is broken down would seem to be related to the shaking up or vibration of the brain consequent to the trauma. When the head is struck the calvarium becomes deformed[9,11] and displaced even if only a fraction of a millimeter, whereas the brain being semi-solid takes up the acceleration more slowly. This produces an area of positive pressure at the point of the blow and an area of negative pressure on the contralateral side which may be demonstrated by the Hamilton manometers with suitable membranes. This

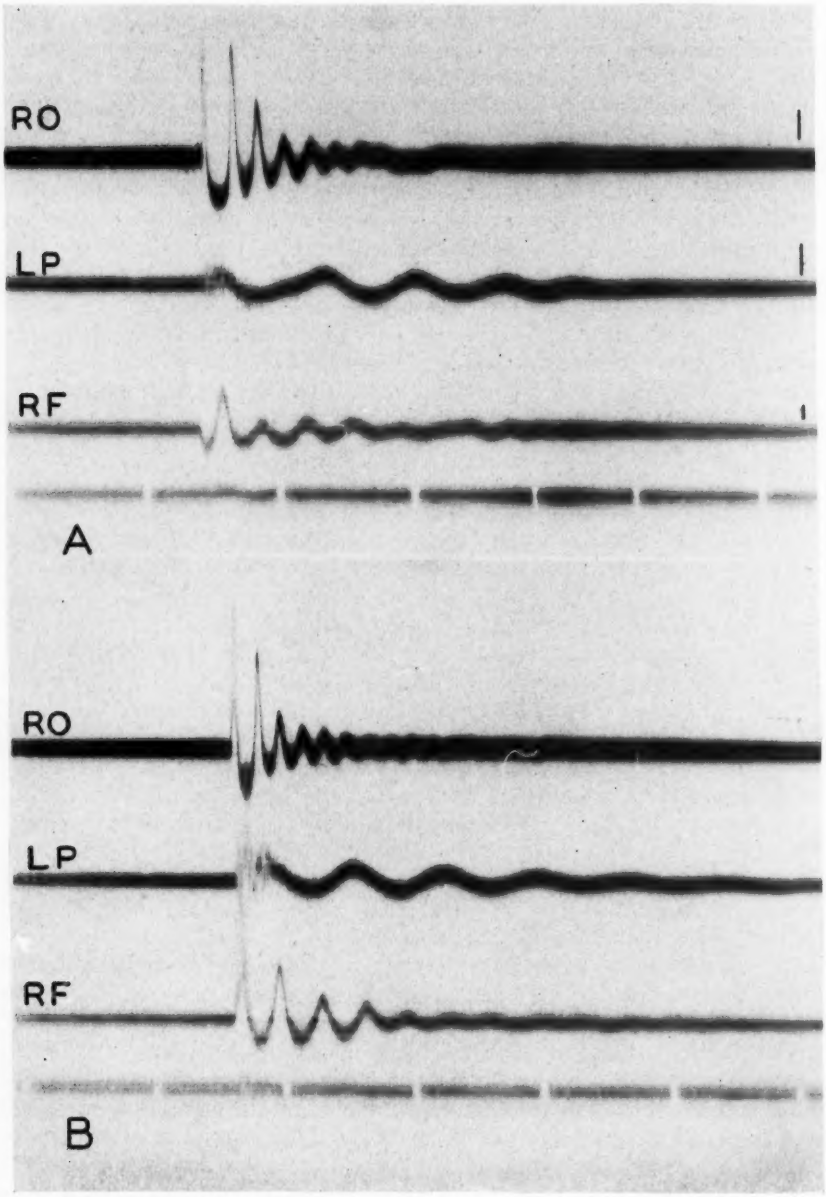


FIG. 6. See next page for description.

asynchronous movement of the skull and brain sets up strong pressure waves which are quickly damped (Fig. 6). That these pressure waves are not the same in all parts of the intracranial cavity probably indicates that the brain must undergo additional stress where the asynchronous waves meet. The actual movement of the brain at the moment of a blow to the head has been beautifully demonstrated by Pudenz and Shelden.[18]

Holbourn[12] states that linear acceleration of the brain producing waves of compression and rarefaction causes little or no damage and that shearing forces produced by rotational acceleration are the main cause of brain injury. Such being the case the pressure waves which have been demonstrated might not play so great a role as those shearing strains occurring mainly at the periphery of the hemisphere, that is, the cortex. This locus of stress has been demonstrated by Ferrari[13] who inserted glass wires within the brain, and found that they were shattered especially at the cortex. However, Courville[2] has emphasized that the rigid falx and tentorium offer resistance to the movement of the brain, and that along their margins more severe trauma is to be expected. Both the linear compression waves and shear strains may be predominately confined to the point of application of the blow, thus producing a local concussion.

While Holbourn's hypothesis of rotational acceleration affords a ready explanation for contrecoup injuries and cerebral lacerations about the sphenoidal ridge in the human brain, it seems likely that in small heads such rotational forces would not be so important. Certainly bruising about the orbital surface of the frontal lobe and tip of the temporal lobe is rarely seen in the cat, dog or monkey as the result of a head injury. Much more commonly, subarachnoid hemorrhage is seen about the base of the brain and petechial hemorrhages in the mesencephalon as if the brain stem were pushed downward into the foramen magnum. Such a movement of the brain would produce marked shearing forces especially in the brain stem.

Irrespective of which type of force produces the traumatic depolarization of the cell membrane there is now evidence that powerful pressure waves are set up within the intracranial cavity by a blow on the head and that the frequency and force of these waves vary in different parts of the calvarium. It should be emphasized that it is not the pressure developed by these waves that is the important factor but the rapid oscillations in pressure. We have slowly increased the intracranial pressure to levels comparable to those seen

FIG. 6. Intracranial pressures in the anesthetized cat as recorded by the Hamilton manometer showing the difference in the wave pattern with the head movable (*A*) and fixed (*B*). The head was allowed to move in the first instance only 2 cm., being arrested by a backstop. The blows were struck in the left occipital region by a hammer weighing 630 g. having a velocity at the moment of impact of 2.294 m. per sec. in *A* (9.6 ft. per sec.), and 3.133 m. per sec. in *B* (10.2 ft. per sec.). The first blow produced a momentary concussion, the second a severe concussion. The records were made on the same animal with an interval of 34 minutes. The vertical lines at the right-hand side represent a calibration for 300 mm. of mercury. (The abbreviations are as follows: RO, right occipital cannula; LP, left parietal cannula; RF, right frontal cannula.) (Time is indicated in tenths of a second on the baseline.)

in concussive blows for 1 to 2 seconds without producing the concussive syndrome.

One further factor, which is more concerned with the sequelae of concussion, should be mentioned. By the breakdown of the cell membrane the permeability of the cell wall is altered and electrolytes pass freely to and from the cell. This undoubtedly modifies the water balance of the tissues and cells, and probably is at the basis of the cerebral edema, which White *et al.*[24] find after concussion. Although the breakdown probably lasts only milliseconds, it is conceivable that under certain circumstances it may persist ten seconds or longer, in which event secondary factors such as anoxemia, hypoglycemia (Dixon[6]), edema, and acid pH, loss of electrolytes and the accumulation of lactic acid will further impede the recovery of the neuron. These sequelae of cerebral concussion are probably the basis of traumatic unconsciousness lasting more than a few minutes and for the symptoms of dizziness, confusion and headache which develop with the return of consciousness.

DISCUSSION

Many theories have been advanced to explain cerebral concussion. The majority of these hypotheses held that cerebral anemia produced by one means or another was responsible for the syndrome. This method by which the cerebral anemia was considered to be induced was variously described as due to reflex stimulation (Miles[17]), or momentary compression of the brain (Kocher[13]). Scott[21] was the first to demonstrate that a marked rise in intracranial pressure was produced by a blow on the head. All previous work, and some subsequent studies had been carried out with recording systems inadequate to register rapid changes in the intracranial pressure lasting only a few thousandths of a second. The accumulating evidence (Denny-Brown and Russell[5]), suggested that concussion was due to a direct mechanical effect on the nerve cell. But the result was generally considered to be paralytic, and Trotter[22] states that concussion "manifests widespread symptoms of a purely paralytic kind." A few investigators have noted evidences of stimulation but have endeavored to explain them on a paralytic basis. Thus Denny-Brown and Russell[5] conclude that concussion is "an immediate traumatic paralysis of reflex function" but add "in reaching the above definition, we have neglected the respiratory and vasomotor mechanisms. If, however, maintained inspiratory spasm and loss of expiration are accepted as evidence of paralysis of the respiratory center . . . ."

This analysis has demonstrated that both the clinical manifestations and electrical accompaniments of cerebral concussion indicate that the process is one of excitation of large masses of neurones within the central nervous system. It is therefore suggested that the physiological basis of concussion consists of the traumatic discharge of the polarized cell membranes of the neurons of the central nervous system by the shaking up or commotion of the brain and that the subsequent course of events is that which would be expected when large masses of nerve cells discharge, such as is seen in the

spontaneous or electrically induced convulsive seizure. The concussive syndrome is then to be looked upon as excitatory rather than paralytic, the latter being merely the normal physiological sequelae of the primary intense stimulation termed "extinction" by Dusser de Barenne and McCulloch.[8] That all degrees of concussion may occur is readily understandable on the basis of this theory of concussion. A local concussion of the brain may occasion a brief dazed feeling comparable to a petit mal attack. Certainly the stars seen after a blow to the head rest upon the same physiological basis as the unformed visual hallucinations induced by the stimulating electrode applied to the striate cortex. Thus we conceive of cerebral concussion as the traumatic excitation of nervous tissue, producing in its wake the train of electroencephalographic, chemical and clinical findings which are known to characterize intense stimulation of the nervous system by electrical, chemical or other agents.

SUMMARY

Analysis of the clinical manifestations of concussion in the cat, dog and monkey show that they are the result of intense excitation of the central nervous system at the moment of the blow to the head.

At the moment of concussion a marked electrical discharge occurs within the central nervous system. In the vinethene-novocaine anesthetized animal the cortical activity is increased in frequency following the initial discharge (afterdischarge) for 10 to 20 seconds, then decreases until there is little spontaneous activity (extinction). Within several minutes the electroencephalogram becomes practically normal again.

At the moment of a blow on the skull a sudden increase in pressure at the site of impact occurs with pressure waves being transmitted throughout the intracranial cavity.

It is concluded that these mechanical forces produce a breakdown of the polarized cell membranes of many neurones in the central nervous system, thus discharging their axones. This intense traumatic excitation is followed by the same electroencephalographic, chemical and clinical phenomena which characterize intense stimulation of the nervous system by electrical, chemical or other agents.

REFERENCES

1. Cannon, W. B. Cerebral pressure following trauma. *Amer. J. Physiol.*, 1901, *6:* 91–121.
2. Courville, C. B. Coup-contrecoup mechanism of craniocerebral injuries. *Arch. Surg., Chicago, 45:* 19–43.
3. Cushing, H. Concerning a definite regulatory mechanism of the vasomotor centre which controls blood pressure during cerebral compression, *Johns Hopk. Hosp. Bull.*, 1901, *12:* 290–292.
4. Denny-Brown, D., and Russell, R. Experimental cerebral concussion. *J. Physiol.*, 1940, *99:* 153.
5. Denny-Brown, D., and Russell, R. Experimental cerebral concussion. *Brain*, 1941, *64:* 93–184.
6. Dixon, K. C. Mechanism of cerebral concussion. *Lancet*, 1940, *2:* 360.
7. Duret, H. Commotions graves, mortelles, sans lésions (commotions pures) et lésions cérébrales étendues sans commotion dans les traumatismes cranio-cérébraux. *Rev. neurol.*, 1920, *35:* 888–900.
8. Dusser de Barenne, J. G., and McCulloch, W. S. Factors for facilitation and extinction in the central nervous system. *J. Neurophysiol.*, 1939, *2:* 319–355.

9. FÉLIZET, G.-M. Recherches sur les fractures du crâne. (Thesis.) *Paris: A. Delahaye*, 1873, 167 pp.
10. GOODWIN, C. W. A differential amplifier for resting and action potentials of biological systems. *Yale J. Biol. Med.*, 1941, *14:* 101–106.
11. GURDJIAN, E. S., and WEBSTER, J. E. Experimental and clinical observations in the mechanism of head injury. *Res. Publ. Assn. nerv. ment. Dis.*, 1943, *24*. (In press)
12. HOLBOURN, A. H. S. Mechanics of head injuries. *Lancet*, 1943, *2:* 438–441.
13. KOCHER, T. Hirnerschütterung, Hirndruck und chirurgische Eingriffe bei Hirnkrankheiten. In: *Nothnagel's Specielle Pathologie und Therapie*. Wien: A. Hölder, 1901, 9 (3), 457 pp.
14. KREMS, A. D., SCHOEFFLE, G. M., and ERLANGER, J. Nerve concussion. *Proc. Soc. exp. Biol., N. Y.*, 1942, *49:* 73–75.
15. LORENTE DE NÓ, R. Analysis of the activity of the chains of internuncial neurons. *J. Neurophysiol.*, 1938, *1:* 207–244.
16. MEYERS, R. Cortical extinction in convulsions. *J. Neurophysiol.*, 1941, *4:* 250–265.
17. MILES, A. On the mechanism of brain injuries. *Brain*, 1892, *15:* 153–189.
18. PUDENZ, R. H., and SHELDEN, C. H. Movie demonstration at the meeting of the Association for Research in Nervous and Mental Disease, New York, December 18, 1943.
19. RANSON, S. W., and HINSEY, J. C. Reflexes in the hind limbs of cats after transection of the spinal cord at various levels. *Amer. J. Physiol.*, 1930, *94:* 471–495.
20. ROSENBLUETH, A., and CANNON, W. B. Cortical responses to electric stimulation. *Amer. J. Physiol.*, 1942, *135:* 690–741.
21. SCOTT, W. W. Physiology of Concussion. *Arch. Neurol. Psychiat. Chicago*, 1940, *43:* 270–283.
22. TROTTER, W. On certain minor injuries of the brain. *Lancet*, 1924, *1:* 933–939.
23. WEBSTER, J. E., and GURDJIAN, E. S. Acute physiological effects of gunshot and other penetrating wounds of the brain. *J. Neurophysiol.*, 1943, *6:* 255–262.
24. WHITE, J. C., BROOKS, J. R., GOLDTHWAIT, J. C., and ADAMS, R. D. Changes in brain volume and blood content after experimental concussion. *Ann. Surg.*, 1943, *118:* 619–634.
25. WILLIAMS, D., and DENNY-BROWN, D. Cerebral electrical changes in experimental concussion. *Brain*, 1941, *64:* 223–238.

THE RESULTS OF SURGICAL REMOVAL OF PROTRUDED LUMBAR INTERVERTEBRAL DISCS

BURTON M. SHINNERS, M.D. AND WALLACE B. HAMBY, M.D.
University of Buffalo School of Medicine and the Buffalo General Hospital, Buffalo, N. Y.

(Received for publication January 31, 1944)

SINCE 1934, when Mixter and Barr[6] elaborated the clinical syndrome of protruded intervertebral discs, low back pain and sciatica, the advances in all phases of the problem have been phenomenal. Varying opinions have been expressed as to the results obtained by treatment and these have ranged in tone from unduly optimistic to needlessly pessimistic. Claim adjustors of at least one insurance company are known to discourage compensation patients disabled by this lesion from seeking surgical relief.

In reporting the first 40 cases operated upon for this lesion, Barr[1] found the percentage of relief striking. Twenty-nine patients were relieved of pain. Of these 8 were able to resume all usual activities without residual difficulty; 9 were restricted by residual discomfort to lighter work, but otherwise were well.

In 1941 several opinions were recorded concerning the results of treatment. Barr and Mixter[2] had found that patients were more improved if spinal fusion was done at the time of laminectomy. Of 94 patients with proved ruptured intervertebral discs, who had been followed for at least a year, 77 per cent were relieved completely of sciatic pain. In an additional 18 per cent, only minor pain persisted in the leg. Two patients had proved recurrences. Relief from back pain was not as complete as from sciatic pain. After laminectomy 52 per cent, and after laminectomy and fusion 73 per cent were relieved of back complaints. The rest had complaints of back pain or weakness of varying severity. In 20 proved cases in which compensation was involved, 9 (45 per cent) considered themselves fully recovered, 6 were doing lighter work, and 5 were still receiving compensation. In the same year, Dandy[3] reported that he had seen no recurrences in his patients. Echols[4] followed up 40 of 50 patients: 29 were classified as having had successful results, 8 improved and 8 unimproved.

In 1943, VerBrugghen[7] reported the results of 66 patients followed up in a group of 75. They were classified as excellent (15 per cent), good (68 per cent), fair (11 per cent), and poor (6 per cent).

In the same year, Love and Walsh[5] wrote concerning the results in 750 cases. The mortality rate was less than 0.25 per cent and the rate of recurrence approximately 2 per cent in the lumbar region. They stated that complete relief of symptoms should occur in 80 per cent of cases. A "small group" of patients continue to have backache, although relieved of their sciatic pain.

We have made an attempt to determine the symptomatic relief provided patients by removal of protruded intervertebral discs in the period

between 1937 and July 1943. The shortest period following operation was six months.

MATERIAL

The material consists of all cases explored surgically for a protruded intervertebral disc from 1937 to July 1943, in all stages of the development of our knowledge of this lesion. There were 140 patients explored, and 160 operations were performed, 20 patients having two operations. There have been no fatalities and one mild wound infection. In 116 patients protruded discs were found at the first operation. In 8 patients recurrences were subsequently found at the same level. In 3 patients second disc protrusions were found at a new level. These total 127 examples of disc protrusion. Twenty-four of the 140 patients (17 per cent) were explored without discovery of disc protrusions.

Of the 116 patients with disc protrusions, 85 were men and 31 women.

The ages of the patients, grouped in decades, were: *11–20 yrs.* 3, *21–30 yrs.* 19, *31–40 yrs.* 49, *41–50 yrs.* 34, *51–60 yrs.* 11.

Two of the discs were in the cervical, 3 in the dorsal, and 111 in the lumbar region. The lumbar levels were: *L–I* 1, *L–II* 2, *L–IV* 34, *L–V* 74.

TYPES OF OPERATIONS USED

The first 9 patients were subjected to more or less complete laminectomy. Thereafter (July 24, 1939 to Jan. 18, 1940) hemilaminectomy was employed. On Jan. 18, 1940 our first interlaminal approach was made and this operation has been employed since, except in a few cases where local bone configuration necessitated a larger exposure. In September 1939 we began implanting a silver hemostatic clip as deeply as possible into the disc sinus in the hope that recurrences would be signalled by a change in the position of the clip. This proved true on two occasions. This procedure was suggested in 1937 by Barr.[1] Since September 1943 a small amount of tantalum powder has been placed in the disc sinus in 12 selected cases for the roentgenographic visualization of the extent of the disc defect. This will be commented upon in a later report. At Dr. Dandy's suggestion the disc sinus has been curetted routinely since June of 1942.

Spinal Fusions. It has been the general impression that sciatic pain is relieved by removal of a disc protrusion in a greater percentage of cases than is back pain. This has led to the question of the advisability of and the criteria for spinal fusions upon these patients. Some surgeons suggest a routine fusion of some type in all such explorations, while others find no occasion for fusion. On our service the orthopedists see the majority of the patients and if the back is frankly unstable, a fusion is done by the orthopedist at the initial operation. Otherwise it is done only when the simpler operation has proved ineffective.

Of 140 patients whose backs have been explored, 18 have been fused. Thirteen of these fusions were done in the group of 116 patients from whom disc protrusions were removed, and 5 in the 24 patients explored without

finding disc protrusions. Eight of the fusions were done at the first operation (7 with and 1 without disc protrusions) and 11 at subsequent operations (7 with and 4 without protrusions).

Spinograms. Lipiodol, air, oxygen and thorotrast were used as roentgenographic contrast media in this series extensively until about November of 1942. At that time practically all contrast studies were abandoned since it was realized that the results were not only confusing but often misleading. In 91 of these 140 patients 100 spinograms were done, some patients having several such studies, occasionally with different media. Table I shows an analysis of results of these studies:

TABLE I

100 Spinograms		*100 Spinograms*	
Lipiodol	47	Proven correct	69
Air	36	False positive	20
Thorotrast	17	False negative	11

47 lipiodol spinograms	Correct	34—72.0%
	False positive	9—19.0%
	False negative	4— 8.5%
36 air spinograms	Correct	22—61.0%
	False positive	9—25.0%
	False negative	5—14.0%
17 thorotrast spinograms	Correct	13—76.0%
	False positive	2—11.8%
	False negative	2—11.8%

RESULTS OF OPERATIONS

Method. Since all patients were not available for followup examination the data were gathered from questionnaires returned by the patient. To allow the patient to interpret his own reactions, these were simply-worded sheets made in the following form:

Dear ———— Date: ————

I am interested in finding out the results of the operations performed on some of my former patients. With this in mind, I am sending you this mimeographed letter hoping that you will answer the questions and return it to me.

1. Please put an *X* in Front of *One* of these Statements:
   I think the operation cured me.
   I think the operation helped, but did not cure me.
   I think I am about the same as before the operation.
   I think I am worse than I was before the operation.
2. Did you feel relieved of pain before you left the hospital?————
3. When did you begin feeling better?————
4. Do you still have pain?———— If so, describe what it is like.————
   ————
5. Are you working?———— When did you return to work?————
   a) What kind of work are you doing?————
   b) What kind of work did you do before the operation?————
   c) What kind of work did you do before your trouble started?————

d) Are you getting compensation now?_____

e) Does working bother your back?_____ Your legs?_____

6. Are you worse in any way than before the operation?_____
If so, please tell how._____

7. If you are not well, are you in any way better than you were before the operation?_____ Please tell how._____

8. In general, are you glad or sorry you had the operation?_____

Thank you for your help.

Very truly yours,

Among the 111 patients having disc protrusions producing low back pain and sciatica, 87 responded, 9 could not be reached by questionnaire and 14 did not reply. The figures in Table II are based on the 87 responses:

TABLE II

43	(49.5%)	consider themselves cured.
42	(48.3%)	consider themselves improved.
2	(2.3%)	consider themselves in some way worse than before operation.
87	(100.0%)	
47	(54.0%)	have some residual pain in the back, leg, or both.
76	(87.4%)	are working, only 4 having changed occupation.
5 of 24		compensation patients (20.3%) still receive compensation.
49	(57.3%)	have pain in leg or back on working.
80	(92.0%)	are glad they had the operation.
4	(4.8%)	are sorry, for various reasons, that the operation was performed. Two were silent on this point.

Results after Spinal Fusion. Seven patients had spinal fusion, because of orthopedic indications, at the time of the original operation when disc protrusions were removed. Of these 5 responded to the questionnaire and were free of pain and working; 2 did not reply. These figures alone are unfairly optimistic; one of these patients broke her fusion and had a recurrence of disc protrusion, required re-fusion and, because of subsequent pain, a rhizotomy finally was necessary before relief was obtained. Another required reoperation and rhizotomy, and relief was obtained only after about three years of suffering. Five patients were not relieved by the removal of disc protrusions and required secondary fusions. Of these 3 have been relieved by the fusion and the second operation in two has been done too recently to evaluate results. Two patients had recurrent disc protrusions with fusion at the second operation; their fusions, also, were done too recently for evaluation.

Five patients in whom no disc protrusion was found at the first operation have had fusions; only 2 of these are relieved of their pain, one probably because the fusion did not hold. Perhaps these 5 patients should not be mentioned in this report, but their pain was sufficiently suggestive of a disc protrusion to require its investigation and 2 spinograms were falsely positive.

Results after Negative Exploration. Of the 140 patients explored surgically, 24 (17 per cent) were found not to have disc protrusions as a cause of their

pain. As mentioned in the preceding paragraph, 5 of these patients had spinal fusion, with relief in two cases. Thirteen of the 24 patients answered the questionnaire. Nine of the 13 (69 per cent) have had sufficient relief to cause them to consider the operation worthwhile. The ultimate result in this group of patients is not so good as their hospital progress would cause one to anticipate.

Results in Patients Receiving Compensation. It has been a general impression that patients receiving compensation for sequelae of disc protrusions received at work have less satisfactory results from surgery than do private patients. Table III is a comparison of these two groups:

TABLE III

Total Discs Removed 116	*Compensation Patients* 33 (28.4%)	*Private Patients* 83 (71.5%)
Replies 87	24 (73.0%)	63 (76.0%)
Cured	10 (41.5%)	33 (52.3%)
Improved	12 (50.0%)	30 (47.6%)
Non-committal	1 (4.2%)	—
Worse	1 (4.2%)	1 (1.5%)
Residual pain	13 (54.0%)	34 (54.0%)
Pain caused by work	14 (58.0%)	35 (55.6%)
Working now	18 (75.0%)	58 (92.0%)
Still receiving compensation	2 (20.8%)	—
Glad the operation was done	22 (92.0%)	58 (92.0%)
Sorry the operation was done	1 (4.2%)	3 (4.8%)
No answer	1 (4.2%)	1 (1.5%)

Table III reveals a striking percentage parallel between the two groups answering the questionnaire. It indicates that any essential difference probably is that private patients are forced to continue work in spite of their complaints, while patients on compensation are relieved of that necessity. It shows, also, that 75 per cent of compensation patients are removed from the compensation rolls following surgical removal of their protruded discs.

SUMMARY

A questionnaire survey was made of the results of surgical treatment of protruded intervertebral discs. In 140 patients 116 disc protrusions were found at the first operation, 8 recurrences later occurred at the same level and 3 at new levels. Twenty-four patients were explored without finding disc protrusions.

An analysis was made of the value in diagnosis of 100 spinograms of various types.

The rôle and results of spinal fusion are discussed.

Listed are the results obtained after simple removal of disc protrusions, after spinal fusion and after exploration without disclosing a protrusion.

A comparison is made of results in private and compensation cases; these are strikingly parallel.

REFERENCES

1. Barr, J. S. "Sciatica" caused by intervertebral-disc lesions. A report of forty cases . . . , *J. Bone Jt. Surg.*, 1937, *19:* 323–342.
2. Barr, J. S., and Mixter, W. J. Posterior protrusion of the lumbar intervertebral discs. *J. Bone Jt. Surg.*, 1941, *23:* 444–456.
3. Dandy, W. E. Concealed ruptured intervertebral disks. *J. Amer. med. Ass.*, 1941, *117:* 821–823.
4. Echols, D. H. The neurosurgical treatment of sciatic pain. With notes on 50 consecutive cases. *New Orleans med. surg. J.*, 1941, *94:* 265–270.
5. Love, J. G., and Walsh, M. N. Protruded intervertebral disks. *Surg. Gynec. Obstet.*, 1943, *77:* 497–509.
6. Mixter, W. J., and Barr, J. S. Rupture of the intervertebral disc with involvement of the spinal canal. *New Engl. J. Med.*, 1934, *211:* 210–215.
7. Verbrugghen, A. H. Herniated nucleus pulposus. A report of 75 cases . . . , *Dis. nerv. Syst.*, 1943, *4:* 165–177.

PERIPHERAL NERVE SURGERY—DIAGNOSTIC CONSIDERATIONS*

CLAUDE C. COLEMAN, M.D.
Department of Neurological Surgery, Medical College of Virginia, Richmond, Virginia

(Received for publication February 26, 1944)

THE DIAGNOSIS of peripheral nerve lesions depends primarily on a precise knowledge of the regional anatomy. The surgical anatomy of the extremities does not receive the attention in teaching of medical students and internes that its importance deserves. The writer has received the impression from years of teaching medical students and resident staff officers that there is a regrettable lack of knowledge not only as to the function of peripheral nerves but as to their physical appearance and anatomy. Interne assistants frequently express surprise that the median or ulnar nerve when exposed by operation at the wrist is so large. They have been under the impression that the nerves are more or less minute structures and difficult to recognize. Fortunately, there has been a trend in recent years toward better surgical training in conditions affecting the extremities but much remains to be done in this direction.

Study of nerve lesions by clinical and experimental methods shows great activity during times of war but if one may judge by the American literature in the interval between the First World War and the present conflict there is little evidence of a sustained interest in these important injuries. It is true that some valuable contributions, such as those of Stookey, Davis and Pollock, appeared in the interval between the two World Wars but on the whole the subject was rather generally neglected and this in spite of the fact that nerve lesions produced by industrial and transportation accidents in civilian life are by no means uncommon. They are easy to recognize but too often inadequately treated.

The clinical examination of the patient supplies the most important information as to peripheral nerve injuries. Clinical diagnosis, however, has received many accessions from careful experimental investigation. It is the purpose of this paper to discuss primarily the clinical diagnosis of peripheral nerve lesions, with brief reference to certain research methods as have proven helpful in advancing clinical diagnosis.

There are definite effects which follow a lesion of every peripheral nerve. The interpretation of these effects in a given case requires precise knowledge of the motor distribution of the nerve as well as its cutaneous sensory supply. While there are numerous effects of division of a large peripheral nerve, loss of motor power in the muscles supplied by the nerve and associated loss of sensation are by far the most serious results.

---

* Presented at the meeting of the American Academy of Orthopaedic Surgeons, Chicago, Illinois, January 22 to 26, 1944.

In the diagnosis of nerve injuries, one must take into consideration the type of injury, the primary effects upon muscle function and sensation in the nerve field, the level of the lesion, and the interval between injury and examination. There are numerous other considerations but time permits discussion of only the more important ones.

Division of nerves in civilian practice most frequently results from cuts by glass or sharp instruments. One of the most common peripheral nerve injuries in civilian practice is that of the median or ulnar or both of these nerves at the wrist. With such injuries there is usually a severing of important tendons. Unfortunately the treatment of these very serious injuries is often delegated to an inexperienced interne, notwithstanding the fact that proper repair of such lesions requires the services of an expert surgeon. In the treatment of these injuries by the inexperienced operator, the median and ulnar nerves frequently are not identified, nerves are often confused with tendons and suture of the median to the palmaris longus tendon or the ulnar to the flexor carpi ulnaris tendon is not infrequent. I feel quite sure that this deplorable error has been discovered by many neurological surgeons at secondary operation.

The immediate loss of nerve function following a stab wound or penetration by fragments of glass in the region of the nerve is unequivocal proof that the nerve has been divided either partially or completely. A stab wound or glass cut about the parotid region resulting in immediate inability to close the eye on the injured side or inability to retract the corner of the mouth means that one of the main branches of the facial nerve has been severed. The diagnosis of nerve division in this type of injury is easy if one bears in mind this simple fact. The failure to make a correct diagnosis early and to carry out proper surgical treatment in any nerve injury due to sharp instruments is most unfortunate inasmuch as there is inevitable retraction of the nerve segments and formation of neuromas, making later direct suture more difficult and sometimes impossible. In median and ulnar lesions, delayed nerve repair allows for the development of advanced atrophy of the intrinsic hand muscles, periarticular fibrosis and other crippling effects which permanently mar the results of later suture.

We are more concerned at the present time with nerve lesions produced by gunshot wounds of the extremities. The diagnosis of nerve lesions in such conditions must take into consideration certain concussional effects of missiles of high velocity which may cause a temporary interruption of nerve function without serious structural damage to the nerve itself. In other words the concussion from a projectile of high velocity passing near the nerve may cause a temporary physiological interruption of nerve function. However, the loss of function is not as complete as is the case when the nerve trunk itself is directly damaged. The nerve lesion produced by gunshot may not divide the nerve trunk but may cause a lateral defect or a neuroma in continuity from hemorrhage within the nerve trunk, and complete physiological interruption. In nerve wounds of warfare an effort must be made to differ-

entiate clinically between a lesion causing slight structural damage from which the patient may recover spontaneously, and one in which the nerve is severely damaged, requiring suture. To make this differentiation between the recoverable and nonrecoverable nerve lesions is not always easy. In the First World War the problem of diagnosis often was met by delaying exploration of the nerve to test spontaneous recoverability and, in some cases, because of persisting wound infection, this delay was required. However, if the nerve proved to be incapable of regeneration, much valuable time was lost and the delay resulted in further crippling of the motor apparatus from atrophy and other disabling effects of long continued denervation.

In the writer's opinion, a nerve showing complete physiological interruption at the time of complete healing of a wound from gunshot or other missile should be promptly explored to make as precise a diagnosis as possible and to suture those nerves that are found divided. It will generally be found in doubtful cases that the nerve lesion exposed is a more serious one than indicated by the clinical examination. It was the experience in the nerve reconstruction centers of the First World War that in many nerve injuries when there were thought to be signs of satisfactory nerve regeneration there was found complete division with wide separation of the nerve segments and no possibility of spontaneous regeneration.

The early recognition of nerve injuries in war wounds is of greatest importance. Because of the frequency of nerve injuries in war wounds of the extremities, it is essential that examination be made at the earliest possible moment in these cases to determine whether one of the main peripheral nerves has been injured. It is gratifying to know that this is the practice of the Medical Corps in the American Expeditionary Force in the present war. Such an examination should record as fully as practicable the essential facts of a nerve injury. In civilian practice it should be determined if possible in examination of a fractured extremity whether there has been an associated nerve injury or injury to one of the large vessels before treatment of the fracture is instituted. Musculospiral injury is a frequent accompaniment of fracture of the humerus and it should be detected promptly.

While the diagnosis of nerve lesions is primarily clinical, under certain conditions complete diagnosis can be made only by surgical exploration of the nerve. The surgical exposure for more exact diagnosis of peripheral nerve lesions is a fairly simple procedure in experienced hands, but expert surgical judgment may be required when the nerve is exposed to determine the potentiality of the nerve for spontaneous recovery when a fusiform neuroma and not division of the nerve is revealed. The surgical treatment of these lesions after diagnostic exploration will be discussed by Colonel Spurling.

The clinical examination of a patient with suspected nerve injury should be done carefully and systematically. One may well begin this examination by study of the motor function of the unaffected extremity. We find that patients do not always comprehend promptly what is expected of them if asked to perform movements in the paralyzed extremity but if one has the

patient execute first the desired movements of similar muscles on the unaffected side, he will better understand what is expected when the involved extremity is subsequently investigated.

In the study of median, musculospiral and ulnar lesions, the appearance and posture of the hand give very definite information. Paralysis of the ulnar and musculospiral nerves may be recognized at a glance. Certain characteristic effects are wrist drop in musculospiral and *griffe* defect in ulnar lesions with the inevitable deviation of the little finger from the ring finger. There are certain simple well known tests which are useful in the study of all median, ulnar and musculospiral nerves. These tests are based upon loss of muscle power resulting from nerve interruption. The patient with a median nerve lesion at any level is unable to hold the thumb at right angles to the palm. In lesions above the origin of the branches to the long flexors of the digits the patient is unable to flex the distal phalanx of the thumb and index finger. He is unable to appose the pulp of the thumb to the pulp of the fingers and efforts to do so result in the thumb crawling over the palm of the hand. In ulnar lesions the patient can make only feeble lateral movement of the fingers and in no case can he superimpose the little finger on the adjacent ring finger. He may be able to hold with considerable force a sheet of paper between the extended fingers of the unaffected side but he has practically no power to do this on the injured side. In the study of nerve function of the hand one thinks of the median as supplying the thumb primarily, whereas the ulnar serves the refined movements of the fingers with some overlapping in the function of both nerves (Figs. 1, 2 and 4).

The characteristic feature of musculospiral paralysis is wrist drop. While this nerve produces extension of the forearm, complete loss of this movement is unusual due to the fact that the branches to the long head of the triceps leave the nerve at a high level and these branches generally escape injury. If the patient with musculospiral paralysis places the palm on a flat surface he is able to elevate the tips of the fingers through ulnar interosseous action but not the thumb, the extensors of which are supplied by the musculospiral (Figs. 3 and 9).

The study of muscle function following nerve lesions in the lower extremities is by no means so complicated as that of the upper in view of the fact that the muscles of the feet are not normally capable of the refined movements required of the hand. Inability to extend the knee from a lesion of the anterior crural nerve was rarely seen in the reconstruction hospitals of the First World War, due to the fact that when this nerve was injured, the femoral vessels were also divided and fatal hemorrhage occurred.

Flexion of the leg on the thigh is seldom abolished by division of the sciatic nerve inasmuch as some of the branches to the semitendinosus leave the nerve at a high level and escape injury. The principal motor loss due to sciatic injury is inability to perform movements of the ankle joint and toes. When the internal popliteal is paralyzed, plantar flexion is impossible. Dorsiflexion of the foot or raising the toes from the floor when standing cannot

FIG. 1 (*left*). High combined lesion of the right ulnar and median nerves, showing typical appearance of hand. Note the deformity of the right hand as compared with the left.

FIG. 2 (*right*). Complete paralysis of the right median and ulnar nerves from division of the nerves in the upper arm by a fragment of glass. Note flexion of the wrist by substitutionary action of the extensor osseus metacarpi pollicus supplied by the musculospiral. The tendon of this muscle can be seen. The scar of incision is also shown. It was necessary to transpose the ulnar nerve to get satisfactory approximation. The neuromata of the median nerve were tied together by sutures with the forearm in flexion for four weeks. At the end of this time the nerve had been elongated sufficiently to permit satisfactory suture.

FIG. 3 (*left*). Beginning recovery of musculospiral paralysis from a lesion in the arm. The patient is able to accomplish slight elevation of the index finger.

FIG. 4 (*right*). Characteristic deformity of the hand following ulnar nerve lesion. Note the hyperextension of the proximal phalanges due to the unopposed action of the common extensors. Note also the flexion of the terminal phalanges from the pull of the deep flexors of the fingers.*

be performed when the external popliteal is divided. Partial lesions of the sciatic nerve are not uncommon and frequently one of its main constituents may be divided by a projectile while the other escapes injury.

In the study of loss of muscle function due to nerve paralysis, one must keep constantly in mind what is known as supplementary, substitutionary or "trick" movements performed by muscles supplied by the adjoining uninjured nerves when the muscles primarily responsible for the movement have been paralyzed. An interesting example of such a "trick" movement is elevation of the upper extremity to a right angle even though injury to the axillary nerve has produced deltoid paralysis. The writer recalls only one such case in the First World War but two cases have been seen in recent practice.

* Taken from "The interpretation of muscle function in its relation to injuries of the peripheral nerves" (C. C Coleman, *Surg. Gynec. Obstet.*, 1920, *31*: 246–254).

Substitution for the deltoid function in such cases is probably from the combined action of the pectoralis major, supraspinatus and trapezius muscles. In the examination of muscle function it should be determined whether the

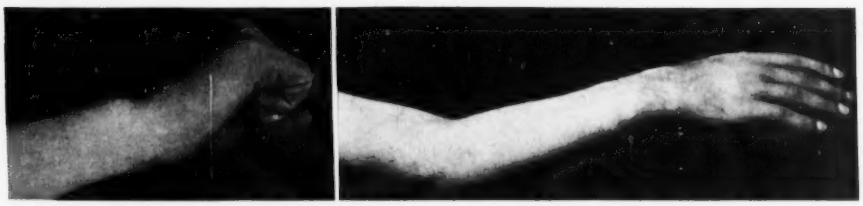


FIG. 5 (*left*). Extension of the wrist in musculospiral paralysis by complete flexion of the fingers. This is not possible when the extensors have been lengthened from unsupported wrist drop.*

FIG. 6 (*right*). Flexion of the forearm by the pronator radii teres in patient with paralysis of the musculospiral and musculocutaneous.*

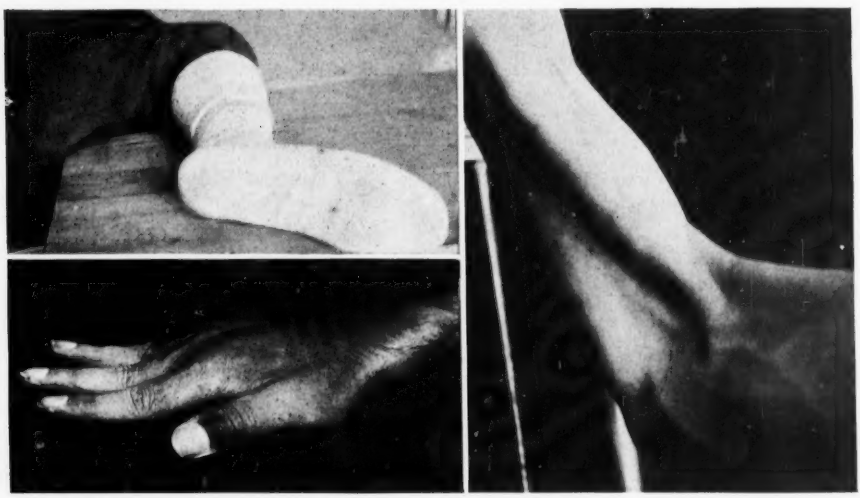


FIG. 7 (*upper left*). A polished exercise-board for patients with recovering paralysis of the flexors or the extensors of the leg. Patients with great weakness of these muscles may show movement of the leg on this board, which is designed to offset the effects of gravity.*

FIG. 8 (*right*). Atrophy of the brachialis anticus.*

FIG. 9 (*lower left*). Musculospiral paralysis. The two distal phalanges of the fingers can be raised from the table by the action of the interossei and lumbricales. Extension of the thumb is impossible.*

muscle which ordinarily produces the movement contracts. This is done by inspection when the patient makes the effort and particularly by palpation of the muscle in question. Palpation, of course, is impossible in the intrinsic muscles of the hand but can be used in the study of action of the larger muscles of the extremities. Another interesting substitution or "trick" move-

* Loc. cit.

ment for flexion of the wrist in high combined lesions of the median and ulnar nerves, in which case all the flexors of the forearm are paralyzed, is flexion of the wrist which may be accomplished by the extensor ossis metacarpi pollicis supplied by the musculospiral, and in some instances we have seen this muscle develop considerable compensatory hypertrophy (Figs. 10 and 11).

Reference should be made to another very important substitution of function in paralysis of the musculocutaneous, which supplies the biceps and brachialis anticus, the primary flexors of the forearm. Here the patient is capable of making rather forcible flexion by action of the brachioradialis,

FIG. 10 (*left*). Paralysis of the right deltoid muscle with marked atrophy. The patient is able to elevate the arm to a right angle by substitutionary action of the trapezius, pectoralis major and supra spinatus muscles.

FIG. 11 (*right*). Paralysis of the right deltoid muscle. The patient is able to elevate the arm to a right angle through substitutionary action, as is shown in Fig. 10. Such substitutionary action for the deltoid was rarely seen among the patients of the First World War, but it is perhaps more common than was formerly believed.

supplied by the musculospiral. Palpation of the paralyzed biceps in such case shows flabbiness and lack of contraction, whereas the brachioradialis will be seen and felt to contract with force.

It should be remembered that the long flexors of the fingers when acting tend to produce approximation, whereas the long extensors tend to separate the fingers. Both of these substitutionary actions may conceal a lesion of the ulnar nerve which is primarily responsible for lateral movements of the fingers. In musculospiral paralysis in which a cock-up splint has been used with resulting shortening of the extensors of the hand, making a fist tends to elevate the hand and conceals the musculospiral paralysis (Figs. 5 and 6).

A differentiation must be made between marked weakness and complete paralysis of muscles. A muscle or group of muscles recovering from paralysis due to nerve injury may be unable to execute a movement when such movement is opposed by the force of gravity. Therefore, in the examination it often becomes necessary in order to obtain a precise idea as to whether the nerve is recovering, to place the limb in such position that gravity will not materially interfere with the interpretation (Fig. 7).

Muscle atrophy is a constant effect of denervation (Fig. 8). This may not always be in proportion to the seriousness of the lesion. Certain irritative le-

sions without serious direct structural damage, particularly in cases of slight blows to the ulnar at the internal condyle, may produce marked atrophy from a traumatic neuritis. Muscle atrophy may result in permanent residual disability, even though a satisfactory suture of a divided nerve has been carried out. This is particularly true in the intrinsic muscles of the hand and regardless of how early nerve suture is done, a certain degree of atrophy remains as a permanent stigma of ulnar nerve lesions.

In nerve wounds of warfare the diagnosis may be more complicated because of multiple lesions of a single nerve. To determine the presence of various lesions at different levels requires a long operative exposure of the nerve trunk for diagnostic purposes.

The diagnosis of traction lesions of a nerve trunk is particularly difficult insofar as determining the extent or level of the neural damage. A traction lesion is most common in the brachial plexus around the shoulder joint, in the external popliteal, and in the musculospiral from fracture of the humerus with wide dislocation of the fragments. In civilian practice, injury to the brachial plexus from blows or falling on the shoulder is a frequent lesion. These lesions, unfortunately, are generally avulsion of the cords of the plexus from the spinal cord. The lower cords of the plexus often remain intact, enabling the patient to make hand movements but without power of movement of any larger segment of the extremity. No form of surgical treatment can benefit avulsion injuries of the brachial plexus.

Investigation of sensory loss following peripheral nerve injuries forms an important part in the diagnosis but it is of secondary importance, in the writer's opinion, to the interpretation of disturbed motor function. There has been much discussion and difference of opinion among neurologists as to the sensory defects following peripheral nerve injuries. Important contributions on the subject have been made by Pollock, who has studied carefully the overlapping of uninjured nerves on the field primarily supplied by the injured nerve. There appears to be an attraction of the denervated skin field for nerve fibers from the surrounding uninjured nerves so that the original field of lost sensation may become very much reduced. The sensory examinations are time-consuming and require much patience on the part of both the examiner and the patient. In view of the fact that intelligent cooperation of the patient is essential to accurately chart sensory loss, the usefulness of this procedure is somewhat limited in many cases.

Reference should be made to studies in electrical skin resistance upon which valuable work has been done by Curt P. Richter of Baltimore. When the peripheral nerve is divided, sweating soon disappears from the area of denervation. The skin in this field then becomes an area of high electrical resistance which is determined by an ingenious apparatus. In order to carry out the test successfully the patient should not be cold and if the examination is conducted with the room temperature low, the patient should be given 1/10 grain of pilocarpine to produce sweating. It will then be possible, according to Richter, to map out within $\frac{1}{8}$ inch a line of demarcation between

the denervated high resistance and the normal field in which the resistance is low. The advantages of this method are at once obvious. It is an objective test which may be carried out without the cooperation of the patient and this may be particularly important in patients with associated head injury. It will be useful in determining between functional or malingering cases and organic lesions. It may also be important in determining the recovery of function, since recovery of sensation and skin resistance coincide to a large extent. I am indebted to Colonel Spurling and Major D. L. Rose for permitting me to observe a demonstration of this test in ulnar nerve lesions at the Walter Reed Hospital. Unfortunately, the apparatus for carrying out these tests is not generally available.

A simple test which was thought to have a considerable degree of infallibility in the early stages of nerve reconstruction in the First World War was called the Tinel's sign. By starting some distance peripherally from the site of the injury and gently tapping the skin upward over the course of the nerve toward the injury, a tingling or formication was produced as soon as the down-growing regenerating fibers were percussed. It was thought by this method one could determine whether the lesion was recovering spontaneously and, if so, the level reached by regenerating axones from the central stump. However, the value of the test was considerably discounted in many cases in which the Tinel's sign showed favorable progress of the nerve and later exploration disclosed the nerve completely separated without the slightest chance of spontaneous regeneration. Perhaps the impact from the stimulated area went through scar tissue to the proximal segment and was responsible for the misleading information. It may be that the Tinel's sign would be of some value after suture of the nerve to determine whether regeneration is proceeding satisfactorily. On the whole, however, the writer's experience with the Tinel's sign is not productive of any great amount of confidence in the test.

Reference should be made to electrodiagnosis. The injuries that present the greatest problems as to treatment are those in which there is complete reaction of degeneration. Electrodiagnosis in its usual application is merely confirmatory of the more important clinical history and findings. Study of the nerve at exploration by the faradic current applied to the nerve above the lesion may give important diagnostic information. If application of the electrode above the injury produces contraction of the muscle supplied by the nerve, obviously one would not remove a neuroma in continuity. However, if there is no response in the muscle, the neuroma is a hard resistant one and there is complete sensory and motor loss in the domain of the nerve, the nerve should be regarded as incapable of spontaneous recovery.

Division of peripheral nerves is rarely followed by pain due to the nerve lesion. Patients with severe partial lesions, however, often develop intractable pain. This condition was described in the studies of patients in the War between the States by Mitchell, Morehouse and Keen and is called causalgia. Patients with this pain may sweat profusely in the field supplied by the in-

jured nerve. The pain is constant and burning. Causalgia is likely to be found more often in the median and the internal popliteal. The diagnosis of causalgia due to vasomotor disturbance may be made by injection of the appropriate sympathetic ganglia with novocaine. This should temporarily abolish the sweating and relieve the pain.

Some confusion in diagnosis of peripheral nerve lesions may result from the presence of ischemic myositis or Volkmann's paralysis. The patient has lost sensory and motor power but fibrosis of the muscles is at once apparent on palpation and loss of sensation does not follow nerve distribution. The differentiation between nerve lesions and ischemic myositis should not be difficult but the two conditions may be associated.

A voluminous literature has accumulated on the study of nerve regeneration. There is general agreement as to the more important aspects of regeneration of divided nerves with almost unanimous endorsement of the Wallerian theory. When a nerve is divided the distal segment, through disconnection with the cell body, degenerates and in this process the axis cylinders disappear. Conducting tubes are formed by the Schwann cells in the distal segment and these cells attempt to bridge the gap between the divided segments of the trunk. Efforts of these cells, however, are obstructed by scar tissue formation between the segments so that the gap is filled by scar and is an impermeable barrier to regeneration. The dominant process of regeneration is inherent in the proximal segment of the divided nerve. This segment degenerates proximally for a few millimeters. The axis cylinders of the proximal segment by retaining their connection with the cell body, under favorable circumstances grow into the pathways provided by the process of degeneration in the distal segment. The down-growing axis cylinders, through the distal segment, ultimately reach the peripheral field if there has been accurate and careful coaptation of the divided nerve ends with minimal amount of scar tissue at the point of nerve suture.

There are inherent defects of regeneration which should be mentioned. Regardless of the care taken in approximating nerve segments and how successful the surgeon may be in preventing rotation of the nerve, certain fibers originally intended for one domain of the nerve may pass into another, and motor fibers may enter sensory pathways and *vice versa*. The fact that the number of down-growing axis cylinders from the proximal stump in the process of regeneration is greatly increased, enables many of the axis cylinders to find their proper terminals. There is believed to be branching of axones in nerve regeneration so that one axone originally intended for one part of the nerve field may supply several areas. This axonal branching, together with the misdirection of fibers, imposes certain apparently insurmountable limitations on the results of surgical treatment of divided nerves.

PERIPHERAL NERVE SURGERY—TECHNICAL CONSIDERATIONS*

LIEUT. COLONEL R. GLEN SPURLING, M.C., A.U.S.
Neurosurgical Section, Walter Reed General Hospital, Washington, D. C.

(Received for publication February 26, 1944)

IT IS ESTIMATED that 70 per cent of all battle casualties suffer from extremity wounds. It is further estimated that 15 per cent of the extremity wounds (i.e., 10.5 per cent of all casualties) are complicated by injuries to large nerve trunks. Peripheral nerve surgery, therefore, in point of numbers, is the most important military neurosurgical problem.

Every soldier with a serious injury to one of the major nerves is unfit for active combat duty for several months, and in many instances, forever. When anatomical continuity is disrupted, regeneration, under the most favorable circumstances, progresses at not more than 2 inches each month. As an example, a sciatic nerve, severed in the midthigh, requires a minimum of 15 months for regeneration of fibers to their distant terminations. After anatomical restoration of the nerves, comes the long period of reeducation and strengthening of muscles so necessary to full functional activity. Deformities can be prevented by properly applied braces, and, in many instances, the patient can do productive work during the convalescent period. However, care of the paralyzed muscles complicates the problem. It is useless to have nearly perfect regeneration of nerve fibers if the muscles are allowed to atrophy and fibrose so they are no longer capable of responding to motor stimuli. If soldiers with nerve injuries are to be salvaged for further military service and from veteran pension lists of the future, they must receive prolonged expert care under favorable conditions.

Since most nerve casualties will not be fit for combat duty again, the Army had three choices for their disposition: *First*, give them the best possible surgical repair of the lesion and then discharge them to veteran facilities for care. *Second*, keep them in Army hospitals under continuous physical and occupational therapy until maximum recovery has been achieved. *Third*, teach them the principles of physical therapy, especially the care of their muscles and joints, fit them with proper splints and applicances to prevent deformity, return them to a duty status commensurate with their disability, and require them to return for observation to the hospitals where they received surgical treatment at regular intervals not exceeding 90 days.

The Surgeon General of the United States Army, after careful consideration, has elected to pursue the third course. It is still too early to be sure of the wisdom of the decision. From the patient's point of view, it is the best

* Presented at the meeting of the American Academy of Orthopaedic Surgeons, Chicago, Illinois, January 22 to 26, 1944.

solution, for it restores him to a productive status without seriously jeopardizing the perfection of his recovery.

GENERAL PRINCIPLES OF NERVE REPAIR

The Wound. Experience in our own Army, as well as in the Armies of our Allies, indicates that battle wounds should not be closed primarily even though débridement can be accomplished under favorable conditions. As a result of this policy, many peripheral nerve casualties arrive in the zone of the interior with open granulating wounds—most of them mildly infected. Before the days of chemotherapy, it was considered the best surgical practice to wait at least 3 months after healing before performing elective operations.

During this war considerable modification of these practices had slowly evolved. Now at the Walter Reed General Hospital, the mildly infected wound is closed by secondary suture as soon as the granulating surface is reasonably clean—sometimes a few days after admission. Two weeks after secondary suture, if healing has been satisfactory, repair of the nerve is attempted keeping the new incision as far removed as possible from the recently infected field. This practice is making possible repair of severed nerves earlier than ever attempted before in war time.

Chemotherapy. Sulfadiazine in sufficient amounts to produce a blood level of approximately 5 mgms. per cent is given to all patients with recently infected wounds for 48 hours prior to operation. This level is maintained for a minimum of 10 days postoperative. The operative wound is frosted lightly with sulfanilamide crystals, care being taken to prevent an accumulation of crystals around the nerve trunks. Not more than 5 grams of sulfanilamide are used in any case.

Condition of Joints. In all cases where end-to-end suture is contemplated, it is desirable to have complete mobility of contiguous joints, for it is only by positioning them that extensive defects can be overcome. A high percentage of extremity wounds with nerve injuries have also bone and joint injuries and, in most instances, casts will have been applied. A favorable position for the injured joint or bone may be an unfavorable one for nerve repair; therefore, before operation is attempted, joint mobilization by all means available should be undertaken.

Hemostasis. Careful hemostasis is especially important in peripheral nerve surgery. A wet field with the inevitable swelling that accompanies it is incompatible with consistently good results. It should be unnecessary to state that a tourniquet is seldom necessary or justifiable in operations upon peripheral nerves unless there is an associated lesion of one of the major blood vessels.

Freedom from Tension. When large gaps are to be overcome, excessive tension at the suture line is by far the most difficult problem; yet, to compromise with this principle means inevitable failure. Freedom from tension in many cases can be accomplished only by extensive dissection of the proxi-

mal and distal ends of the severed nerve and by positioning contiguous joints to shorten the course of the nerve. In other cases, transplantation of the nerve may be necessary. In most major nerve trunks, gaps of from 3 to 4 inches can be overcome by correct dissection, transplantation and joint positioning and still leave the anastomosis free of tension.

When motor branches must be sacrificed in order to relieve tension, due consideration should be given to the handicap produced and the possibility of combating it at a later date by appropriate tendon surgery.

Electrical Stimulation of the Exposed Nerves. Electrical stimulation of the exposed nerve trunk is valuable in determining its anatomical continuity. Galvanic, faradic or sinusoidal current provides a satisfactory stimulus. The minimal current is that which will produce a visible contracture of muscle fibers when the electrodes are applied directly to them. The current should be increased 4 or 5 times above this minimal level before deciding that there are no functioning fibers passing through the involved segment.

If stimulation proximal to the scarred area causes contraction of muscles normally innervated by the nerve distal to the scar, it may be assumed that there is still anatomical and physiological continuity of the motor fibers.

If stimulation of the nerve proximal to the scar fails to elicit motor responses even with five times the minimal stimulus, it may be assumed that anatomical continuity is lost, providing the nerve has been liberated from its extrinsic scar prior to the test.

If the operation is conducted under local anesthesia and no procaine has been infiltrated into the proximal segment of nerve, information of great value can be obtained from the sensory responses. Stimulation of the scar or neuroma is always painful, more so than stimulation of normal nerve above the scar. Stimulation distal to the scar without sensory response indicates disruption of the afferent fibers unless the amount of current is excessive and overflows into the neuroma.

Sensory responses to electrical stimulation are valuable in cases of re-exploration after suture. Not infrequently, physiologically active sensory fibers can be demonstrated traversing the suture line before any motor fibers have reached their appropriate end-plates.

The Anesthetic. Infiltration procaine anesthesia is the method most commonly used at the Walter Reed General Hospital in the peripheral nerve cases. Where there have been extensive wounds with dense, widespread scar formation, local infiltration anesthesia may not be completely satisfactory. In these circumstances, either inhalation ether or continuous spinal anesthesia is used.

Indications for Exploration. Preoperative clinical and laboratory studies of motor, sensory and vasomotor functions will indicate usually the degree of physiological disruption of a peripheral nerve. However, there can be *complete physiological loss of function* without *anatomical severance of the nerve.* This fact explains the frequency with which injured peripheral nerves regenerate spontaneously. Because of the likelihood of spontaneous regene-

ration, some surgeons have recommended a waiting period of from 6 to 9 months before advising exploratory operations. However, most recent investigators believe that the degenerative changes which inevitably occur in the denervated muscles are progressive and that the best results are obtained in those cases where repair is accomplished early, therefore waiting for spontaneous regeneration is unjustifiable[9].

The policy presently followed in this clinic is to explore *all* cases of peripheral nerve palsies, complete or incomplete, unless there has been rapid, progressive improvement of symptoms. If the nerve has been severed, valuable time has been saved by early repair. If the nerve is anatomically intact, freeing it from the surrounding scar tissue will usually hasten recovery, and seldom retard it. It is believed that exploration of any major nerve trunk under proper conditions can be accomplished without risk to life or to function.

The policy of radical exploration, however, should always be combined with one of conservative treatment once the nerve is exposed. Unless actual anatomical division can be demonstrated, or unless the intrinsic scar is so dense that no motor or sensory impulses can be demonstrated to pass through the scar, only complete neurolysis should be done. Clinical experience and laboratory experiments[15] have shown that regeneration through a crushed segment of nerve is often more nearly complete than can be obtained by end-to-end suture. If a nerve thus treated fails to show evidence of regeneration within 2 months, re-exploration is done, and if there are still no sensory impulses passing through the scarred area, resection with end-to-end suture is undertaken.

All cases of suture—or neurolysis for that matter—should be observed carefully week by week for evidence of new functional activity. If at any time satisfactory progress seems to have stopped, re-exploration should be recommended.

The value of the Tinel's sign in diagnois has been discredited by many observers because of the frequency with which percussion impulses can be transmitted through scarred soft tissue to a distant neuroma. If the percussing stroke is heavy no doubt the jarring will invalidate it. The sign should be elicited by very gentle tapping with the finger tips along the course of the nerve, always working from below the lesion upward. At the point where tingling in the peripheral distribution is produced, functioning sensory fibers are believed to be present. The Tinel's sign when performed properly is a valuable one, especially in following the progress of regeneration after suture.

OPERATIVE TREATMENT

The Acute Lesion. The following quotation from a recent directive to all military surgeons from the Surgeon General's Office gives the present status of treatment of acute nerve injuries in the Army:

> Primary nerve suture should be done when the nerve-ends are readily accessible and can be approximated without tension. If this is not possible, and the injured nerve-ends are

identified, a sling suture of fine stainless steel wire should be placed between them, or they should be anchored with similar suture material to the surrounding tissues in order to prevent retraction. The use of metal suture material here is desirable because it permits roentgenographic identification for subsequent repair. In view of the irreparable degenerative changes that occur in the end-plates of severed nerves, early repair of these nerves is absolutely essential. For this reason, it is of the utmost importance to evacuate these patients as soon as possible to the zone of the interior where operative repair and the necessary postoperative physical therapy can be instituted.

Probably the optimal time for the repair of a severed nerve is at the original débridement. Conditions of warfare make this impossible in the vast majority of instances. It is extremely important, however, that at the first débridement, the injured nerve be visualized and the anatomical situation with respect to it be noted on the record. Such information is invaluable to the surgeon who must undertake the repair at a later date.

Not infrequently, there is local contusion of the nerve trunk without actual severance, and in some cases an intrinsic hematoma forms at the site of contusion. Prompt evacuation of the hematoma through a slit in the perineurium in line with the nerve fibers may be followed by early restoration of function.

A recent dramatic example of such a lesion occurred at the Walter Reed General Hospital. The patient sustained severe contusions about the elbow in an automobile accident, and an immediate complete ulnar nerve palsy resulted. Exploration of the nerve 2 hours after injury demonstrated a large intrinsic hematoma. Immediately following evacuation of the clot, motor and sensory symptoms improved and within 24 hours, all functions had been restored to fully 50 per cent of normal. Had the hematoma not been evacuated, the nerve fibers might have been destroyed by pressure or by subsequent fibrosis within the perineurium.

The Subacute Lesion. Approximately 60 per cent of all peripheral nerve cases treated at this hospital also have bone or joint injuries. In those cases with compound fractures, appropriate treatment of the broken bone is of first importance. In those with extensive soft tissue loss, infection and the necessity for large pedicle skin grafts may delay the treatment of the nerve injury for several weeks or even months. Most of the cases, however, are ready for exploration 3 months after injury. Only rarely have operations been delayed longer than 6 months.

During the 12-month period, January 1, 1943 to January 1, 1944, there were 133 patients with peripheral nerve injuries operated upon by the neurosurgeons of the Walter Reed General Hospital. In this group there were 42 end-to-end sutures, 67 neurolyses with or without transplantation of the nerve, 5 nerve grafts (4 homogenous and 1 autogenous), 9 excisions of amputation neuromas and 10 explorations where no remedial pathological conditions were found.

The location of the injured nerves is interesting but perhaps not significant. The arm and shoulder were involved in 69 per cent and the lower extremity in 31 per cent of the cases.

The ulnar nerve was involved 39 times, the median 30 times and the radial but 15 times. This is in striking contrast to the statistics from the last war when all observers found the radial nerve to be more frequently injured than any other major nerve trunks.

In the lower extremity, common peroneal injuries predominated (16 cases), sciatic second (12 cases) and the posterior tibial third (11 cases).

In most penetrating wounds from missiles, particularly where there is a through-and-through wound, the resultant scar about the nerve binds it firmly to the muscles, fascia and bone. After the extrinsic scar has been dissected, the nerve may be found to be intact, even though the muscles in the distribution of the nerve are paralyzed. Sometimes the nerve is remarkably normal in appearance and to palpation, but more frequently it is harder than normal and the external surface is ragged. Electrical stimulation above and below the lesion provides valuable information in such cases and may clearly indicate whether or not the area should be resected and end-to-end suture attempted. If there is the slightest response to electrical stimulation, a conservative course has been followed, particularly if there is minimal intrinsic scarring without neuroma formation.

The practice of injecting normal saline solution into the nerve trunk above and below the lesion with the hope of separating and breaking up an intrinsic scar is a practice which is believed to be both futile and dangerous. The repeated introduction of a hypodermic needle destroys nerve fibers and often injures blood vessels. Furthermore, a scar sufficiently dense to strangulate nerve fibers cannot be destroyed by saline infiltration. Saline injection of the perineurium, however, may be a valuable aid in determining the limits of an intrinsic scar when resection is contemplated.

With both extrinsic and intrinsic scars, a dense firm perineurium is frequently encountered. This fibrous tissue sheath may actually constrict the nerve sufficiently to destroy function. Splitting the perineurium in line with the nerve fibers may have a decompressing effect, and when performed carefully is not harmful and may be of value.

Casts must be applied to all cases after end-to-end suture because the contiguous joints must be kept flexed to shorten the course of the nerve. Such casts are bivalved 24 to 48 hours after operation, or, in some instances, are applied and bivalved preoperatively. Immobilization of the joints is maintained strictly for 2 weeks, although gentle massage and heat are applied after the wound is healed, usually on the tenth postoperative day. Gradual extension of the joints is started after the second week, and full extension is completed by the fifth week.

The Technique of End-to-End Suture. For the past 15 months at the Walter Reed General Hospital, fine tantalum wire has been used to suture peripheral nerves, and the site of anastomosis has been wrapped in a cuff of tantalum foil. Extensive animal experimentations, as well as clinical observations, indicate that tantalum is, for all practical purposes, inert when buried in human tissue.[11,13] Because of its inert qualities as well as its malle-

ability and strength, it has become an important adjunct to peripheral nerve surgery. No other suture material, with the possible exception of human hair, is so free of adverse reactions.

The usual method of end-to-end repair of large nerves with only a series of sutures in the perineurium is open to certain criticisms. Correct apposition at the periphery of the union can be maintained, but the centrally placed tubular structures may separate, particularly if there is tension upon the loose tissues of the perineurium. A sling (traction) stitch placed through the center of the upper and lower trunks and tied with just enough tension so that the tubular structures meet, appears to be the answer to these criticisms (Fig. 1,A–E). The chief objection to the sling stitch in the past has been the inflammatory reaction occurring around the suture material. With fine tantalum wire this objection has been removed. When the sling stitch is tied, great care must be exercised so that the cuff surfaces of the proximal and distal stumps just touch each other. Too much tension on this stitch causes wrinkling of the tubes—too little leaves an undesirable dead space.

After the sling stitch is placed and tied, a series of fine interrupted sutures of .003 inch tantalum wire is placed in the perineurium. Tantalum wire sutures welded to fine curved needles are now available.

In making an end-to-end suture, it is desirable that no twisting of the proximal or distal trunks should occur. To prevent rotation an orientation suture should be placed in the perineurium above and below the lesion before dissection of the ends has been attempted.

To replace a carefully made nerve anastomosis into a bed of scar tissue has always been conceded to be undesirable. Surgeons have resorted to many materials—fat pads, fascial sheets, preserved membranes and excised segments of arteries and veins—in an effort to eliminate or diminish the extrinsic scar. Most of these materials have been abandoned because the resulting fibrosis was seldom diminished and often increased by the would-be protective substance. A cuff of thin tantalum foil (twelve ten-thousandths of an inch in thickness) wrapped around the nerve prevents scar tissue from infiltrating into the nerve trunk. It has been clearly demonstrated[13] that a non-inflammatory membrane resembling peritoneum forms on either side of the tantalum foil. Also, movement within the cuff has been demonstrated in the human by measuring the position of the metallic sutures within the cuff on roentgenograms, after changing the position of the contiguous joints.

In applying the cuff, a number of precautions must be observed. *First*, the foil must be smooth and unbroken or fibrous tissue will grow through every little tear and fix the nerve firmly to the surrounding scar. The foil may be annealed by wrapping around an obturator, inserting the obturator with its covering of foil into the sheath and heating the whole assembly in a flame until the sheath just begins to glow. We have used a large ventricular needle with its stylet as an obturator for this purpose. Thus treated, the foil maintains a firm spring curl and is much easier to apply to the nerve without wrinkling. *Second*, the cuff is held in place by two circular ties of

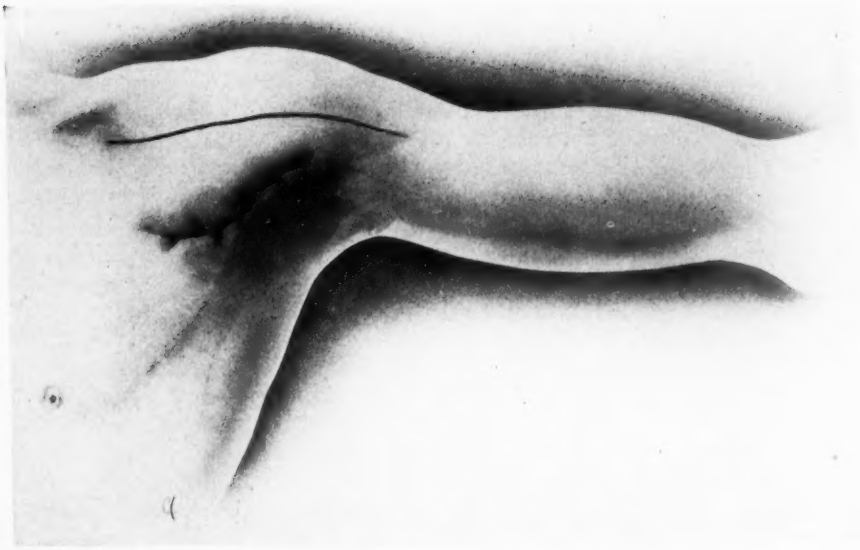


FIG. 1-A. Line of incision used for exploration of axillary portion of brachial plexus. Note healed gunshot wound in anterior axillary fold.

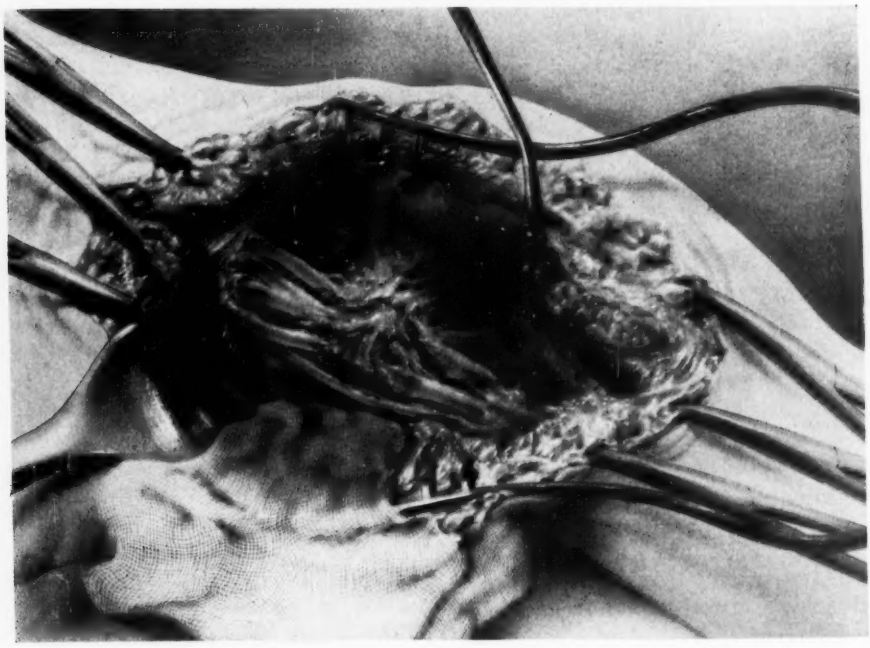


FIG. 1-B. Brachial plexus exposed. Note dense scarring of plexus. The axillary artery had previously been ligated.

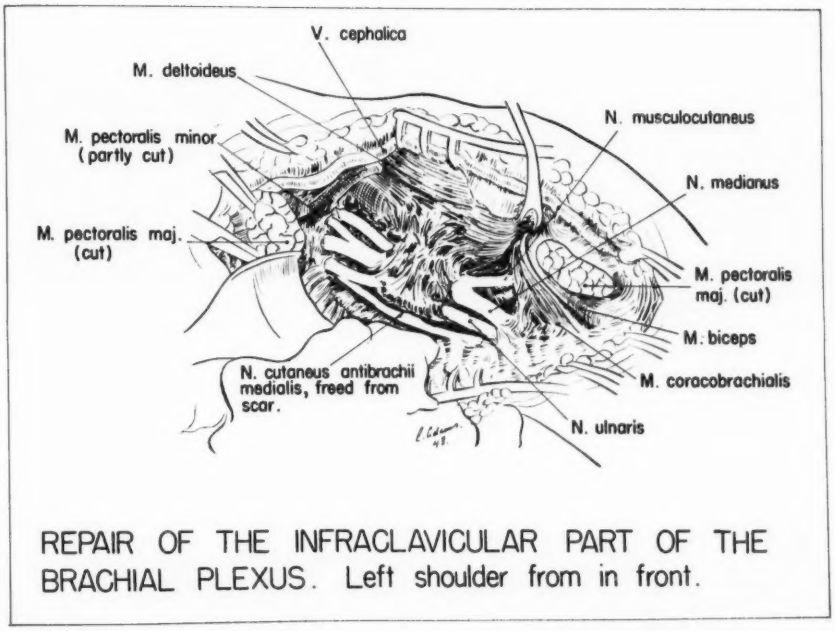

V. cephalica
M. deltoideus
M. pectoralis minor (partly cut)
M. pectoralis maj. (cut)
N. musculocutaneus
N. medianus
M. pectoralis maj. (cut)
M. biceps
M. coracobrachialis
N. cutaneus antibrachii medialis, freed from scar.
N. ulnaris
REPAIR OF THE INFRACLAVICULAR PART OF THE BRACHIAL PLEXUS. Left shoulder from in front.

FIG. 1-C. Key explanatory sketch for Fig. 1-B.

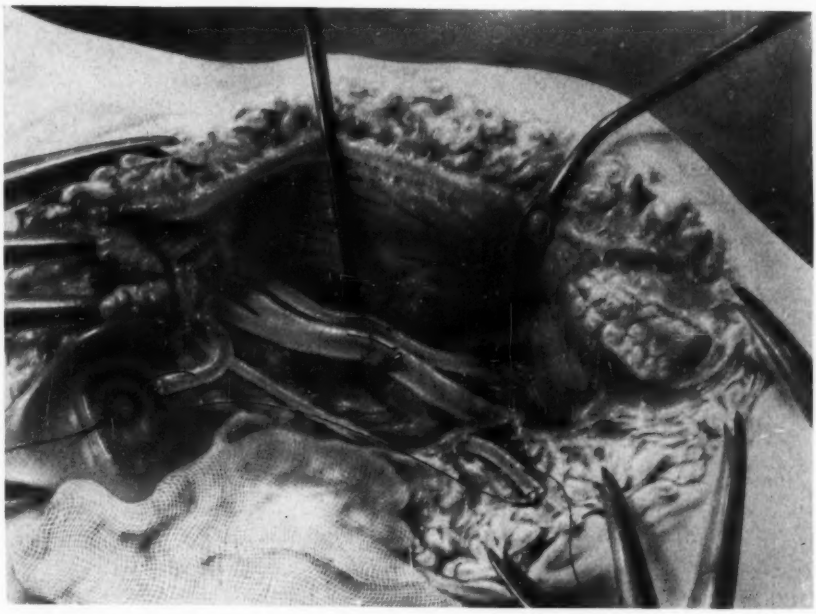


FIG. 1-D. After resecting scar end-to-end sutures of the musculocutaneous and median nerves completed with sutures of fine tantalum wire. The sling stitch in the ulnar nerve has been placed.

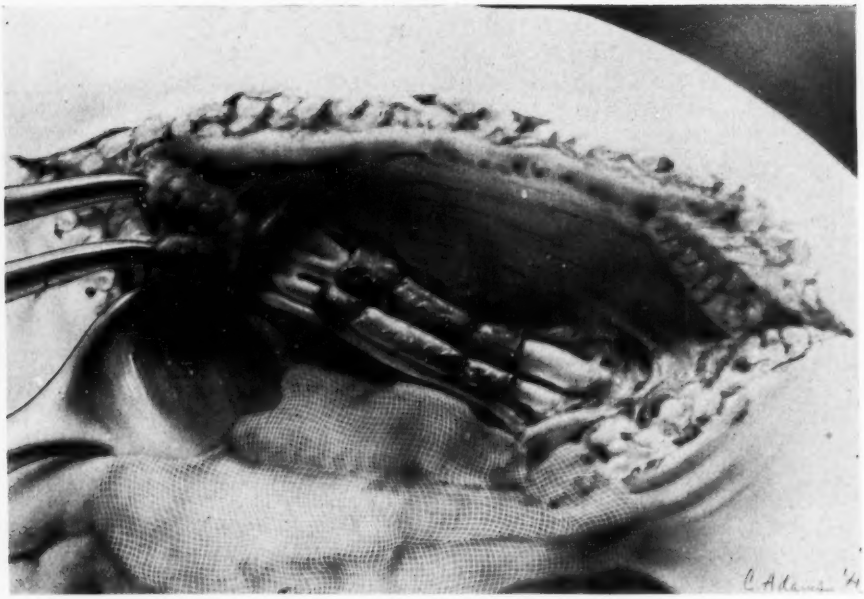


FIG. 1-E. Anastomotic areas wrapped in cuffs of tantalum foil tied loosely with 00000 plain catgut.

00000 plain catgut. In the beginning, fine tantalum wire was used, but it was found undesirable because with the growth of fibers the cuff over the lower segment must be able to expand. The wire tie below the point of anastomosis was drawn too tightly in two cases and regeneration stopped at this point of construction and was resumed only after removing the wire tie.

The length of foil cuff is determined by the extent of the surrounding scar. On several occasions a cuff 4 inches in length has been used, although in most instances 2 inches will suffice.

It is very important that the central stump of the severed nerve should be trimmed until normal appearing nerve bundles appear. Likewise, the distal stump should be trimmed until well formed bundles of Schwann cell tubes are evident. There can be no compromise with these trimming procedures, for unless the anastomosis is made of tissue free of scar, the operation is doomed to failure.

Brisk bleeding from the stumps always occurs. It is best controlled by placing a hemostatic substance, either a bit of free muscle or a piece of human fibrinogen foam saturated with clotting thrombin, on the end of the nerve. These hemostatic substances must be removed before suture is attempted.

In many instances, it will be found necessary to transplant the ends of the severed nerve to a new anatomical environment in order that tension on

the suture line may be reduced. This is particularly true of the ulnar and radial nerves where transplantation is relatively simple and effectual.

Incomplete division of a nerve is not infrequently found. If the anatomically intact part contains functioning fibers then every effort should be made to save this part while repairing the divided part. It is often possible to separate the nerve into two parts by longitudinal dissection, making an end-to-end suture of the severed portion and leaving the intact portion coiled free in the tissues.

In certain cases where it is impossible to do a primary end-to-end suture without tension, the two-stage method may be effective. In the first stage, the neuroma and the pseudoneuroma are tied tightly together with .005 inch tantalum wire after the contiguous joints have been placed in extreme flexion. The extremity is immobilized in a cast, and after 2 weeks, gradual extension of the joints is started, thus automatically stretching the nerve. When full extension is reached, the wound is re-explored, the neuromas excised, and, again, tension relieved by flexing the joints, after which an end-to-end suture is performed in the usual manner. In most instances, this two-stage method is preferable to an immediate nerve graft, although there is considerable danger of widespread destruction of fibers in the central portion by over-stretching.[5,6,8,12]

Nerve Grafting Procedures. Fortunately the number of cases of nerve injury with loss of tissue so extensive that end-to-end suture by one method or another is impossible, are relatively few. Yet, they do occur and some attempt to bridge the gap must be made. Some surgeons have recommended shortening the extremity by bone resections to permit end-to-end suture as a solution to the problem.[3] However, there are relatively few injuries to major nerve trunks where such procedures are practical.

Recent experimental work[4,7,14,15] indicates that in experimental animals autogenous nerve grafts of short length are not far inferior in results to end-to-end sutures. However, nerve grafting operations in humans have been most discouraging. This is particularly true of results reported from the last war.

The most brilliant clinical results of human nerve grafting have been achieved in the repair of the facial nerve and of the small nerves of the hand.[2] Apparently, small nerves recover function much more completely after grafting than do the larger nerve trunks.

Autografts undoubtedly have given the best results, although homografts are not far inferior. It is always an easy matter to obtain autografts for small nerves, but to obtain an autograft for a large nerve trunk is seldom practical.

Alcohol or formalin fixed homografts have been tried repeatedly and some evidence has accumulated[10] to indicate that there may be an occasional recovery. However, in the opinion of most observers, fixed grafts provide only a bridge for the growth of Schwann cell fibers, and the graft itself disappears by phagocytosis or becomes incorporated in scar tissue from the host.

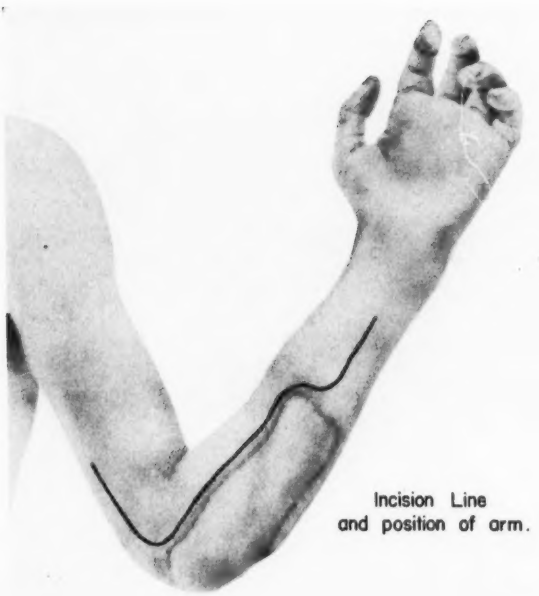


FIG. 2-A. Area of soft tissue loss about the elbow repaired with pedicle skin graft. Note line of incision for nerve suture in relation to the skin graft.

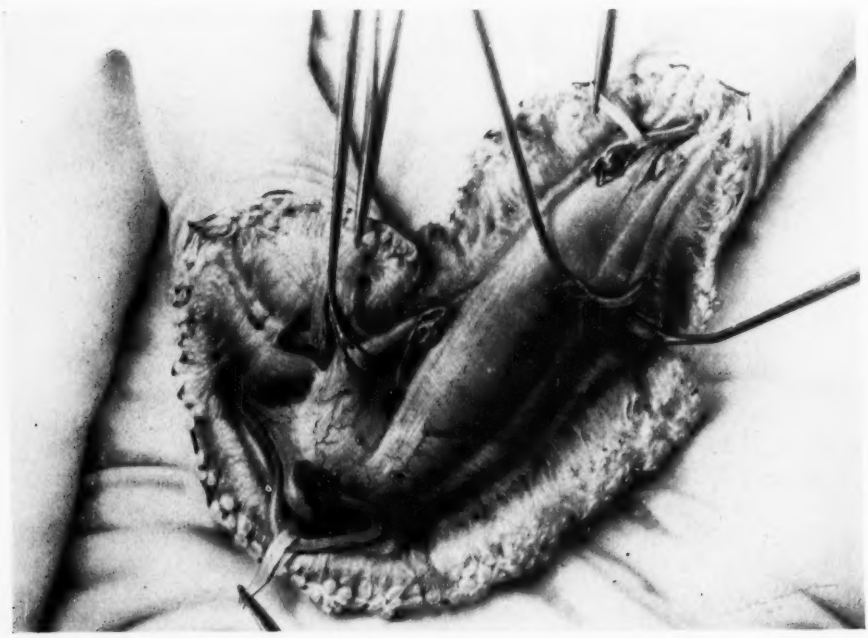


FIG. 2-B. Drawing illustrating anatomical condition of ulnar and median nerves secondary to machine-gun fire.

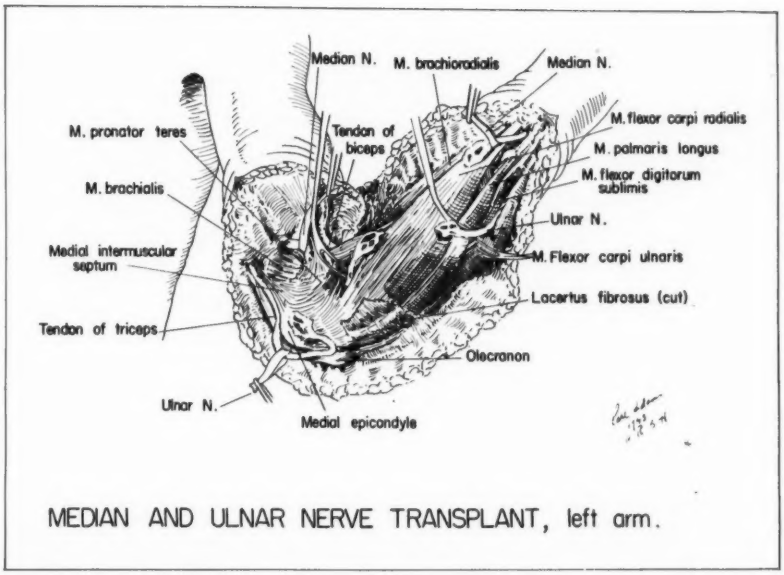


FIG. 2-C. Key explanatory sketch for Fig. 2-B.

FIG. 2-D. After resecting scarred nerves and neuromas gaps of three inches remained.

FIG. 2-E. Gaps in ulnar and median nerves repaired with homogenous grafts obtained from an amputation stump undergoing revision. Median nerve graft completed with tantalum foil cuffs in place. Ulnar nerve graft sutured and cuffs will be applied about suture lines.

After considering the problem from all angles, it has been elected to confine the nerve grafting operations at the Walter Reed General Hospital to fresh homografts, although there is no evidence at the present as to their success. One reason for this decision is the abundance of material available from the amputation service, where stumps are being revised in large numbers.

There have been five such operations performed during the past year. The suture technique employed has been similar to that used in end-to-end suture, namely, the anastomosis is made with fine tantalum wire and the site of anastomosis is surrounded by a small cuff of tantalum foil (Fig. 2, A–E).

NERVE IRRITATION—TRAUMATIC NEUROMAS

Many incomplete nerve injuries are associated with causalgic-like pain and may be relieved by dissection of the extrinsic scar or the removal of foreign bodies. Neurolysis in such cases is usually followed by slow progressive improvement of symptoms, and if the nerve must be replaced into a bed of scar tissue, a protective cuff of tantalum foil is used. Minor causalgias from nerve irritation should not be confused with other types of causalgia and phantom limb. These major cases form quite a different problem, and surgical procedures directed toward the peripheral nerves are seldom beneficial.

Painful amputation stumps are due frequently to neuromas on the ends of the severed nerves. With the guillotine type of amputation in particular, the nerves are often incorporated in the scar, and the whole mass is fixed to the end of the bone. The pain of traumatic neuromas is characteristic; it is produced only by pressure, and it radiates into the normal distribution of the nerve. It is relieved by novocain injection at the site of the neuroma.

Neuroma formation on the central end has generally been considered inevitable after sectioning a nerve trunk. There is considerable evidence, however, to indicate that under certain conditions, neuromas may be prevented. [1,12] In an attempt to prevent neuroma formation, two types of procedure have been used. The first one consists of burying the central stump of the nerve into the medullary cavity of the most accessible long bone. Four such cases have been operated upon with satisfactory clinical results. The second procedure used consists of wrapping and fixing of the central stump of the nerve into a tantalum foil sleeve. Two cases have been operated upon by this method. One of them was re-operated upon after two and a half months and no evidence of neuroma formation could be demonstrated. The clinical results in these two cases have been completely satisfactory. However, insufficient time has elapsed to evaluate the effectiveness of either procedure.

REFERENCES

1. Boldrey, E. B. Presented at the annual meeting of the American Academy of Neurological Surgery, Chicago, Ill., 1942.
2. Bunnell, S., and Boyes, J. H. Nerve grafts. *Amer. J. Surg.*, 1939, *44:* 64–75.
3. Dandy, W. E. A method of restoring nerves requiring resection. *J. Amer. med. Ass.*, 1943, *122:* 35–36.
4. Gutmann, E. Factors affecting recovery of motor function after nerve lesions. *J. Neurol. Psychiat.*, 1942, *5:* 81–95.
5. Gutmann, E., and Sanders, F. K. Functional recovery following nerve grafts and other types of nerve bridge. *Brain*, 1942, *65:* 373–408.
6. Gutmann, E., and Sanders, F. K. Recovery of fibre numbers and diameters in the regeneration of peripheral nerves. *J. Physiol.*, 1943, *101:* 489–518.
7. Gutmann, L. Experimental study on nerve suture with various suture materials. *Brit. J. Surg.*, 1943, *30:* 370–375.
8. Highet, W. B., and Holmes, W. Traction injuries to the lateral popliteal nerve and traction injuries to the peripheral nerves after suture. *Brit. J. Surg.*, 1942, *30:* 212–233.
9. Holmes, W., and Young, J. Z. Nerve regeneration after immediate and delayed suture. *J. Anat. Lond.*, 1942, *77:* 63–96.

10. KLEMME, R. M., WOOLSEY, R. D., and DE REZENDE, N. T. Autopsy nerve grafts in peripheral nerve surgery. *J. Amer. med. Ass.*, 1943, *123:* 393–396.
11. PUDENZ, R. H. The use of tantalum clips for hemostasis in neurosurgery. *Surgery*, 1942, *12:* 791–797.
12. SANDERS, F. K. The repair of large gaps in the peripheral nerves. *Brain*, 1942, *65:* 281–337.
13. SPURLING, R. G. The use of tantalum wire and foil in the repair of peripheral nerves. *Surg. Clin. N. Amer.*, 1943, *23:* 1491–1504.
14. WEISS, P., and TAYLOR, A. C. Repair of peripheral nerves by grafts of frozen-dried nerve. *Proc. Soc. exp. Biol., N. Y.*, 1943, *52:* 326–328.
15. YOUNG, J. Z. The functional repair of nervous tissue. *Physiol. Rev.*, 1942, *22:* 318–374.

PERIPHERAL NERVE SURGERY—POSTOPERATIVE REHABILITATION*

CAPTAIN W. M. CRAIG (MC), U.S.N.R.
Surgical Section, U. S. Naval Hospital, Bethesda, Maryland

(Received for publication February 26, 1944)

REHABILITATION of the wounded Soldier, Sailor and Marine is receiving more and more attention of the members of the Medical Departments of the Army and the Navy. Our responsibilities as Medical Officers do not end with the suture of the wound, the setting of a fracture, or the repair of a damaged nerve, but continue until the patient is fit to return to duty or discharge from the service in the best possible physical condition.

Owing to our lack of practical experience we have been interested in the methods used by our Allies and as an example of what can be accomplished I would like to refer to a case described in the British literature. Watson-Jones,[1] in discussing rehabilitation in the Royal Air Force, tells the following story:

An air gunner of the Royal Air Force, a man of proved courage and determination, was admitted to a civilian orthopaedic hospital for the treatment of a torn and displaced semilunar cartilage. Ten months later he was still in the hospital and still totally incapacitated. He asked about the delayed recovery. The diagnosis had been correct and a skillful operation performed without complications. Early treatment had been continued in the physiotherapy department but the muscles of the thigh remained atrophic and weak. The joint had twice been manipulated under anesthesia without improvement. The man's gait was slow and hesitant. He limped. He could not run. He had never tried to run. The medical officer blamed him because "he would not co-operate," because he was disinterested, depressed and resentful. He was depressed, for after ten months the incapacity was more complete than on the day of admission. He was disinterested because, in his own words, "nobody takes any notice and it looks as if it is hopeless." He was resentful because he could not believe the fault was his. Had he not been told that "the nerve to his knee had been cut"?

He was transferred to one of the orthopaedic rehabilitation centres of the R.A.F. Medical Service. He saw the sky, the sea, the open spaces. For many months he had seen only the stone walls of the hospital wards, the stone walls of massage rooms, the stone walls of many corridors. His new surroundings were different. There was a lounge and a writing room, tasteful decorations and flowers, a menu which was varied and excellent, an atmosphere of well-being and contentment. After a few days he smiled. There was sometimes a sparkle in his eye. Within a week he sensed the spirit of optimism. It grew upon him and he was reassured. His difficulties were explained and he was taught special exercises. He learned to walk and then to run. He became an enthusiast and worked hard. He worked in the gym, played on the fields, swam in the pool, cycled on the track. Time raced past, for he was busy. He attended lectures, played billiards and went to concerts. He became bronzed and fit. He laughed and was full of the joy of life. In seven weeks he returned to his unit and to full duty. He forgot about the "nerve in his knee." Ten months total incapacity. Seven weeks full recovery. That is the story of rehabilitation in one air gunner.

* The opinions or assertions contained herein are the private ones of the writer, and are not to be construed as official or as reflecting the views of the Navy Department or the naval service at large.

Presented at the meeting of the American Academy of Orthopaedic Surgeons, Chicago, Illinois, January 22 to 26, 1944.

The experience of the air gunner is not unusual. It is typical of victims of injuries to the extremities. In the hospitals of every country at war, there are many injured men whose surgical treatment has been completed for months but who are incapacitated because of minor disuse changes, because confidence is lacking, because morale has been destroyed. Their bodies have been treated, not their minds. The treatment of fractures has been concentrated upon securing bony union, and the treatment of peripheral nerves concentrated upon end-to-end anastamosis. No treatment has been directed to the tone and volume of muscles, the stability of joints, and the circulation of the limbs. There has been no measurement and graduation of physical activity. There has been no attempt to continue treatment until the patient regained confidence and recognized for himself that recovery was complete.

It is a well-recognized fact that a successful nerve repair may be followed by an incomplete or faulty functional recovery, if the muscles are not properly prepared. Davis, in his monograph, states: "It is unfortunate that many times nerve ends are sutured and no thought is given to what we consider to be of at least as great importance—carefully supervised and persistent physical therapeutic after-care." Many structural and metabolic changes may and do take place in the denervated group of muscles. This is especially true when there is associated destruction or trauma to the contiguous structures, such as the muscles, the long bones and the joints. Every traumatized extremity should be treated as a unit and the peripheral nerves should be carefully considered from the standpoint of a functional return. Disabilities resulting from injuries to the radial, median and ulnar nerves, as well as sciatic, tibial and peroneal nerves should be analyzed, and any treatment instituted should include every means to insure a good functional final result. The activation of denervated muscles by passive or active motion, as well as electrical stimulation, increases the metabolism and the circulation of the muscles, and keeps them in much better physical condition, and therefore much more receptive to re-inervation. Although it is difficult to measure accurately, it is an accepted fact that those patients who receive physical therapy show evidences of recovery of function much earlier, and the degree of recovery is much greater, than those who do not.

Physical therapy should be carefully supervised because atrophied, denervated muscles may be injured by rough methods and fatigue. In many cases better results are obtained by simple devices and games which effect an unconscious and effortless exercise of the contracted muscles.

Massage and passive motion have long been used to take the place of active exercise. If massage is to be of service in cases of nerve suture it must be used skillfully at the right time.

The preoperative treatment of peripheral nerve injury cases should be carried out very carefully and should comprise all of the various forms of massage. In the preoperative stage, massage and exercises should be used to keep joint and muscle senses intact, to maintain full mobility or to restore it if lost, to encourage the fullest activity in muscles capable of contraction, and to devise movements and exercises to maintain the vitality of the part as a whole. In the Peripheral Nerve Centers in England during the postoperative treatment of peripheral nerve injuries, skilled masseurs initiate

treatment about a wound with sutures still in place, and massage started at this time may prevent the formation of scars. This type of massage is very delicate, and any abuse tends to encourage rather than discourage the scar tissue in its formation. The best results are obtained when treatment is applied early in the critical ten-day period and the ideal time to start is as soon as it is known that sepsis as a result of operation is not likely to occur.

The first effect of massage is a reflex contraction which may cause fatigue followed by a paralytic effect which may defeat the very objective desired. A muscle deprived of its nerve must, sooner or later, make its first contraction during recovery which may be a feeble flicker to the observer, but to the muscle fibres themselves, a violent and severe effort. Thus it is that during the early stages of recovery any successful attempt at contraction may be followed by massage of the same type as that which should be applied during the stages of complete paralysis. In this way a muscle can be encouraged to make this effort a second and perhaps a third time, but the danger lies in encouraging it too much and causing too great a fatigue. Massage should, therefore, be used up to the point at which active movement can be employed since active muscular contraction provides the perfect form of massage. It has been found with regard to exercise that, until recovery is complete, anything and everything which can be devised to exercise the recovering muscles should be prescribed.

Electrotherapy is useful in postoperative treatments only when contractions of the denervated muscles are produced. Judiciously used, electrotherapy may conserve the volume and nutrition of the muscles, and keep the fibres functionally adequate for voluntary movement when regeneration has progressed sufficiently.

The interrupted galvanic and sinusoidal currents manually or mechanically interrupted, waved or surged currents of low voltage, are often very useful for the production of muscular contractions. They may frequently be employed interchangeably with the interrupted or surged faradic current. The sinusoidal currents are more comfortable than the surged faradic currents for production of such stimulation. They are often useful in initiating muscular contractions before the patient is capable of producing such contractions voluntarily, and they may be employed to teach a patient how to perform voluntary muscle exercises for individual muscles. A few simple modifications of the three basic currents, that is, the interrupted galvanic, the slow sinusoidal, and rapid sinusoidal currents, are all that is required for adequate therapy.

Just as the purpose of massage, exercises, and electrotherapy is to maintain the nutrition of the denervated muscles, the first aim of mechanical splints should be to prevent overstretching of the paralyzed muscles. The ideal splint should be light, simple, easily applied and removed, inexpensive and as inconspicuous as possible. The character of the splint required depends also upon the time which has elapsed between the original injury and the institution of treatment.

When a purely motor or mixed motor and sensory nerve has been divided and its conductivity lost, the muscles supplied by it lose their tone. This allows the joint on which they normally act to assume an abnormal position due to the action of the opponent muscles. The deformity is not due to the loss of tone of paralyzed muscles but rather to a combination of this with the force of gravity. In injuries to the radial nerve there is a very characteristic "wrist drop" or inability to extend the wrist. If the forearm and hand were held continuously in full supination with the elbow at right angles, gravity would act as a dorsiflexor, and its force would be sufficient to counteract the pull of the unbalanced flexor muscles of the forearm. In this position of dorsiflexion the paralyzed extensor muscles would be relaxed, which is the ideal condition for a resumption of function if and when the conductivity of the nerve has been restored. To overcome the position and relaxation of paralyzed muscles, adequate splinting should be used.

When a group of muscles is paralyzed by injury to its motor nerve, deformity may result in the joint on which it acts, and if such a deformity remains uncorrected, secondary contraction occurs in the opposing group of muscles, thereby preventing even passive restoration of the normal position. It is essential that the muscles supplied by the injured nerve be maintained in a position of relaxation until normal function has been resumed. Clinical evidence indicates that the optimum angle for recovery of the muscles is a neutral position at which return of voluntary power appears at the earliest possible moment.

Although splinting plays no part whatever in the regeneration of the peripheral nerve, it is important so far as muscle function and the prevention of deformity are concerned. An overstretched muscle will not regain its contractility even though its nerve supply may be restored completely. According to the reports from Great Britain, six types of splints are required: (1) the abduction splint for brachial plexus injuries; (2) the knuckle duster splint for ulnar paralysis which maintains flexion of the metacarpal phalangeal joints and encourages the patient to keep the interphalangeal joints extended; (3) the splint for median paralysis, and (4) the combined median and ulnar splint which is an elaboration of the knuckle duster; (5) radial paralysis splint to overcome wrist drop, and (6) the splint for sciatic paralysis to overcome foot drop.

Splinting can be overdone. The function of a splint is to prevent paralyzed muscles from being stretched, not to fix joints. Unless contra-indicated, the joints of a paralyzed limb should be put through a full range of movement once daily. If the movement is carried out with care the paralyzed muscles will not be stretched to a harmful extent. If some stiffness is present the range of movement should be increased by passive movement. Gentle manipulation under anesthesia is permissible if not too severe.

There is one phase in the rehabilitation of peripheral nerve injuries which most physicians have completely ignored. This consists of tendon transplantation for paralysis of muscles due to lesions of peripheral nerves.

One of the conditions where this is indicated is paralysis of the muscles supplied by the radial nerve. This procedure is employed when suture of the severed radial nerve is impossible or when function does not return after repair. In injuries of the radial nerve above the level of the origin of the posterior interosseous branch the tendon of the flexor carpi-radialis muscle is inserted into the three extensors of the thumb, and into an extensor of the index finger. The flexor carpi-ulnaris tendon is transplanted into the extensors of the remaining three fingers, and the pronator radii teres is transplanted into the tendons of the extensor carpi-radialis longus and brevus muscles. When the lesion is below the origin of the posterior interosseous nerve the radial extensors of the wrist are not disturbed, and the tranference of the pronator radii teres muscle is of course unnecessary.

At some of the Peripheral Nerve Centers the tendon transplantation is being used in conjunction with the repair of the divided or injured radial nerve. This obviates the necessity for a supportive splint, and when the nerve has regenerated and the function restored, the tendons can be returned to their normal function. It has been pointed out in the rehabilitation of radial nerve injuries that the patient who has a tendon transplant in conjunction with the peripheral nerve repair can return to duty much earlier and there is no time lost waiting for the nerve to regenerate.

While tendon transplant for paralysis of muscles supplied by the median nerve is usually contra-indicated, Bunnell has described such a technique. The extensor carpi-radialis longus is transplanted from the extensor surface of the wrist into the flexor pollicis longus tendon. The profundus tendons to the index and middle fingers are detached proximally and reinserted into the flexor profundus tendons of the ring and little fingers. The flexor carpi-ulnaris may be either inserted into the flexor sublimis tendons to increase the strength of the flexors of the fingers and produce a more central pull on flexion of the wrist, or used as the motor power to produce opposition of the thumb. Steindler replaces the lost opponent action of the thumb by utilizing the flexor pollicis longus muscle provided this structure is active and strong. Royle, on the other hand, transfers the flexor sublimis tendon of the fourth finger into the sheath, and inserts it into the short flexor and opponents tendon at the level of the metacarpo phalangeal joint of the thumb.

Occupational therapy at Peripheral Nerve Centers is a valuable addition to active exercise treatment. In cases of permanent paralysis, it helps develop and improve subsidiary and trick movements. In every case, clear directions should be given to the occupational therapist about the details of motor, sensory and trophic disturbances, and supervision of this therapy by the physician is of great importance. In every case the occupational therapist should record all observations, for these can be of great help to the doctor in evaluating the results of treatment.

The British Medical Association has reported extensively upon rehabilitation and advised that it include (a) functional treatment in hospital wards by regular active exercise, (b) treatment in rehabilitation centers by organ-

ized physical and recreational activities with the object of overcoming residual disuse changes, restoring the confidence of patients in the completeness of their recovery, and bridging the gap between the exercises of the hospital ward and the stresses of normal work; and (c) vocational retraining for the very small proportion of men whose disability is permanent, and who must learn a new trade. Experience has proved conclusively that the demands of rehabilitation are not satisfied by "pepping up the massage department," that it is difficult and usually impossible to fulfill the requirements within the grounds and buildings of a hospital, that a rehabilitation center without the right atmosphere is almost worse than no rehabilitation center at all. The object of functional treatment is not only to cure but also to prevent muscle wasting, joint stiffness and other disuse changes. The treatment must begin as early as possible after the injury and the patient should be kept busy from morning until night. A certain amount of discipline should be maintained and it has been found necessary to organize a rehabilitation team. To every group of fifty patients have been allotted a team consisting of one medical officer, one physical training instructor, and one masseuse. These individuals have been selected for their personality and their ability to command respect and loyalty. The masseuse is engaged not only in electrotherapy and massage, but also in the teaching of exercises and the corrections of the limp. The physical instructors take charge of group exercises, games in the "gym," a limited period of marching and drill, medicine ball or similar activity. At each center there is an organizer of games. The medical officer is responsible for every activity that concerns his own group of patients.

It has been found important to have a large gymnasium with massage, examining rooms and canteen. If possible, it is desirable to have a playing field and a swimming pool. The arts and crafts type of occupational therapy finds its greatest application in the hospital wards where there are many idle hours to fill. Simple workshop activities, such as carpentry, sawing, model airplane construction, and basket or rug making are interesting additions to the rehabilitation center, particularly during the winter months when outdoor activities are limited. Workshops, occupational therapy benches, and massage cubicles are like medicine balls, climbing ropes or equipment which are sometimes useful but never indispensable.

The intention of these rehabilitation centers is that the patients who are capable of ordinary work, for limited periods should use the workshops and at the same time continue treatment. It was also intended that men might be tested from time to time under working conditions, in the same way that an air crew center is equipped with a fusilage by which to test the physical ability of pilots. It has been argued that treatment in rehabilitation centers is unnecessary and wasteful because all injuries fall into one of two groups, the first being those from which full recovery is possible without rehabilitation; and two, those which cause permanent disability despite rehabilitation.

However, it is a well-known fact that it is impossible to assess the degree of permanent disability with any accuracy until a patient has been treated and observed in a rehabilitation center.

Thus rehabilitation begins as soon as the medical officer examines the wounded patient and ends with the return to duty or other disposition of the case. It combines the physiological principles of wound healing, tissue metabolism, circulation, tissue regeneration, and functional recovery. It embraces physical therapy, electrotherapy, splinting and occupational therapy. The object should be the restoration of the injured Soldier, Sailor and Marine to as normal a functioning individual as is possible subsequent to the injuries to which he has been subjected.

REFERENCE

1. Watson-Jones, R. Rehabilitation in the Royal Air Force. In: *Rehabilitation of the war injured*. W. B. Doherty and D. D. Runes, Eds. New York: F. Hubner & Co., 1943, 424–439.

THE TREATMENT OF PAINFUL PHANTOM LIMB BY REMOVAL OF POST-CENTRAL CORTEX*

LT. COLONEL C. G. DE GUTIÉRREZ-MAHONEY, M.C., A.U.S.
Vanderbilt University School of Medicine, Nashville, Tennessee

(Received for publication February 22, 1944)

THE PHENOMENON of phantom limb was probably first recognized and has very likely been seen most frequently by military surgeons. Ambroise Paré[11] recorded the condition clearly in 1551 when discussing amputations in *La maniere de traicter les playes faictes tāt par hacquebutes, et cetera.*† But it was not until 1871 that Weir Mitchell published his article "Phantom limbs"[9] in *Lippincott's Magazine of Popular Literature and Science* and gave us this perfect term which has since had universal usage. He wrote:

> A person in this condition is haunted, as it were, by a constant or inconstant fractional phantom of so much of himself as has been lopped away—an unseen ghost of the lost part, and sometimes a presence made sorely inconvenient by the fact that while but faintly felt at times, it is at others acutely called to his attention by the pains or irritations which it appears to suffer from a blow on the stump or a change in the weather.

In the following year he published his book *Injuries of nerves*[10] and made further observations after studying 90 patients. He not only gave us the details of the various phenomena which the patient experiences in the absent member, but he made very important observations which can be used to explain the sensory ghost and its misbehaviour. He noted:

> If we faradise the track of the nerves in or above the stump, we may cause the lost fingers and thumb to seem to be flexed or extended, and, what is most remarkable, parts of which the man is conscious, but which he has not tried to stir for years, may thus be made to appear to move to his utter amazement. . . . In a case of amputation at the shoulder joint, in which all consciousness of the limb had long since vanished, I suddenly faradised the brachial plexus, when the patient said at once, 'My hand is there again. It is bent all up and hurts me.' It is of course impossible that the motor nerves stimulated should convey any impression centrally, and we must therefore conclude that irritation of sensory trunks may occasion impressions of muscular motion in the sensorium.

The phenomena of the phantom vary in nature and in incidence. Weir Mitchell[10] found that 95 per cent of patients experience phantom limb after amputation, Pitres[13] 97 per cent, Leriche[7] 98 per cent and Foerster[2] 100 per cent. Riddoch[14] noted that pain was referred to the phantom in half of all amputated limbs, but Foerster claimed that pain was experienced in every instance. In our patients it has been almost literally true, as Foerster observed, that pain was felt in every phantom, but it was disabling in very few.

* Read before the eleventh annual meeting of The Harvey Cushing Society, New York City, May 20, 1942.

† Loc. cit. l. 59*a*. "*Car les patientz long temps apres l'amputation faicte disent encore sentir douleur és parties mortes & amputées: & de ce se plaignent fort, chose digne d'admiratiõ, & quasi incredible à gẽtz, qui de ce n'ont experiẽce. Parquoy se fault donner garde, que tel sentimẽt ne nous retarde à faire le debuoir de la parfaicte curation: comme quelque fois i'ay veu couper vn membre à deux ou à trois fois: pour s'estre arresté audict sentiment faux & menteur.*"

The sensations occur much more frequently in the hand than in the foot. They may appear immediately or, more frequently, not until two or three weeks after the operation, although occasionally as long as a year or more may pass before the syndrome develops. Usually only the distal part of the amputated limb is felt, such as the hand or foot, although the whole arm or leg has been removed. In the course of time the phantom recedes and ultimately comes to be attached to the stump. It may move voluntarily or involuntarily; it may be in a constantly cramped state of painful contraction. Frequently it assumes the position of the limb at the time of the amputation. Wounds and parts of the limb previously painful are experienced in the phantom as they were beforehand.

The unpleasant sensations may include undue warmth, itching, or simply the distress due to overconsciousness of the painless phantom. These discomforts may be intermittent but if severe are usually continuous. They are then described as a dull ache or as burning, throbbing, piercing, cramping, sticking, cutting pains. Many patients suffer a deep, agonizing torture due to the sensation of the limb being very tightly compressed, which may be so severe that the victims are willing to undergo any kind of treatment. It has not been unusual for a dozen or more operations, principally amputation of terminal nerve stumps, to have been performed on one patient. Many ultimately have become morphine addicts.

The treatment of the painful phantom has been such an unsatisfactory and disappointing experience that there are very few detailed reports in the literature. Most discussions concern generalities rather than specific records, which is natural, since failure has been the common story. Foerster[3] recorded some of his experiences in 1931 in his paper "Division of the anterolateral tract in man." Two patients with painful phantom fingers whom he treated by high cervical chordotomy and one with a painful phantom foot by upper thoracic chordotomy had only very temporary relief of pain in the phantom. In 1935 he[4] reported five more cases. Two of these had phantom hands and division of all cervical and upper thoracic posterior roots on the side involved gave only transitory relief. Another patient whose arm was amputated at the shoulder was relieved for "eight years" by division of the anterior and posterior roots C-4 through Th-5; "permanent" relief was obtained by another man with a phantom lower limb after dividing the anterior and posterior roots Th-10 through S-5. In a final patient with amputation at the shoulder the posterior roots C-4 through Th-4 were divided and the cervical sympathetic chain was removed including the middle cervical through the second thoracic ganglia. He remained free from pain for many years. Foerster remarked that the combination of posterior root division with removal of the sympathetic trunk was effective in several other cases but did not give details.

No one else has reported the results of combined operations of these types but Leriche[6] used sympathetic interruption, surgical or by infiltration anaesthesia, with some success. The effects lasted for a period of only weeks

or months. Livingston[8] also has had satisfactory results following sympathetic novocaine block.

To present the clinical problem with the vicissitudes of management the following case is brought forward from the records of the late Dr. A. J. McLean.

In September 1932 a man aged 40 developed pain in a phantom arm two weeks after amputation at the shoulder. Three months later the right brachial plexus was explored without relief. Novocaine block of the sympathetic chain was not helpful. In July, and again in August 1932, posterior roots were divided which ultimately included C–5 through Th–3. There was still no relief from pain, and his condition became so unbearable that he was violent at times. In November 1933 while walking in his room his phanton right arm, which was usually felt semiflexed over his abdomen, was pulled outward from his body by great force, raised above his head, and snapped off at the shoulder joint. Then he lost consciousness. His wife saw him half flex the hips and turn his head strongly to the left; after a short period of gasping breath and tonic extension there were clonic motions of the arm and both legs. Following the convulsion the phantom arm was present as before, but the pain had cleared remarkably and he required only very little morphia for a long time. Later the phantom felt as if it were on fire and tied up tight in a straightjacket against his body, utterly incapable of movement. A burning sensation was present all the time in the palm of the hand, wrist and arm. Sharp, excruciating, cutting flashes of pain, lasting for one or two seconds, occurred about every hour throughout the day. These affected the little finger, hypothenar eminence, and the tips of the ring, middle and index fingers. In January 1934 he was first seen by Dr. McLean who did a chordotomy at the level of C–2 on the left. The painful phantom disappeared for a day only to return.

This case is of particular interest, not because of the therapeutic result but because of the convulsion after which the pain in his phantom disappeared. This suggests a temporary interruption of cortical function leading to relief from pain. A similar extraordinary disappearance of a painful phantom was observed after convulsions in another patient in whom a permanent interruption of cortical function was carried out surgically some time later.

Explanations for the phenomena have been proposed by almost everyone who has dealt with this baffling problem. Paré,[11] who made the first suggestion, considered the retracting divided nerves responsible.* Mitchell[10] reproduced the phantom phenomena by electrical stimulation of the nerve stumps, thus emphasizing a peripheral mechanism as the cause. His observations were complemented by Pitres[13] who injected cocaine into the region of the neuromas, thereby stopping the disturbing sensations. More evidence was added by Souques and Poisot[15] who injected cocaine around the terminal scar, causing a constant disappearance of all hallucinations which could not be reproduced by electrical stimulation during the period of anaesthesia. They reported this method for treating the discomforts as well as for inhibiting the involuntary movements of the stump. Thus considerable evidence was accumulated over a period of three and a half centuries which

* Loc. cit. ll. 66*b*–67*a*. "*D'auantage, long temps apres l'amputation faicte, les patientz disent encore auoir la partie qui a esté amputée (cõme i'ay dict) ce qui vient, comme il me semble, à cause que les nerfz se retirent vers leur origine, & en se retirant font grande douleur, & presque semblable aux retractiõs qui se fõt aux spasmes.*"

pointed very clearly to the major rôle played by the peripheral nerve stumps in producing this bizarre syndrome.

The participation of higher centres was recorded by Head and Holmes[5] in 1911. While studying the sensory disturbances which followed cerebral lesions they made the following observation:

> One of our patients had lost his left leg some time before the appearance of the cerebral lesion which destroyed the power of recognizing posture. After the amputation, as in so many similar cases, he experienced movements in a phantom foot and leg. But these ceased immediately on the occurrence of the cerebral lesion; the stroke which abolished all recognition of posture destroyed at the same time the phantom limb.

The part which the autonomic system plays has been emphasized by Leriche and Livingston through relief of pain, although temporary, which has followed interruption of the sympathetic nerves. There were also not a few supporters of a purely psychological explanation. Pick[12] was probably the first of these, and since him others have gone so far as to maintain that the phantom and the associated pain were "a state of mind" without organic basis. Thus the origin and perpetuity of phantom limb have been attributed to all parts of the individual from the skin to the psyche.

FIG. 1. A patient demonstrating with his left hand and arm the position of his right phantom limb after amputation at mid-humerus.

Much psychological discussion has been offered to explain phantoms, but before blaming all on the state of mind of the unfortunate sufferer the simple physiological facts should be exhausted. At this point the decisive observations of Weir Mitchell,[10] Pitres,[13] Souques and Poisot,[15] Head and Holmes,[5] Leriche,[6] and Livingston[8] should not be forgotten, for they demonstrated clearly an organic basis which will explain the pathogenesis of phantom limb—peripheral nerve stimulation reaching consciousness. The vagaries of individual phantoms are beyond immediate analysis. It would be pure speculation to give a reason why a phantom hand gradually finds its way to the height of the amputation, even to the axilla. It is impossible to say why one patient experienced a rough skin on the dorsum of his phantom hand and smooth skin on the palmar side, or why another spoke of his phantom as having a yellow colour. It is also difficult to explain why, although phantoms are experienced universally, not all are painful, and if so, why the pain varies so much in degree and time, even allowing for the inherent differences of the brains in which the peripheral stimuli register. The bizarre nature of the discomforts is also a bit of a mystery but is probably due to the unregulated conglomerate stimuli which assemble in the stump

before marching to consciousness. The various positions which the limb assumes are also not easily explained, a number retaining the posture of the limb at the time of amputation when this has taken place with violence as in warfare or in accidents. The position most frequently described for a phantom upper limb—abduction of the upper arm, flexion and pronation of the forearm, and flexion of the hand and fingers (Fig. 1)—is one which can be reproduced by massive electrical or mechanical stimulation of any one of the large nerve trunks of the arm. Not only do the muscles innervated by the nerve stimulated, be it median, radial, or ulnar, contract, but the entire extremity is moved reflexly so that the upper arm is abducted, the forearm pronated and flexed, and the hand and fingers powerfully flexed. The same reflex movement has been observed immediately after gunshot wounds of large nerve trunks of the arm and has been so forceful as to have remained etched in the memory of the subject. The vividness of the phantom has been explained by Foerster[2] as due to a cortical engraving which was made by the strength of the impulses originating at the time of the amputation or trauma. This engraving then is more readily receptive to subsequent unorganized peripheral stimuli and is prepared to interpret them as previously experienced.

To emphasize the importance of the cerebral cortex, especially the post-central area, in the pathogenesis of the phantom and to demonstrate a method of treatment by extirpation of the proper part of this area, the following case is presented, an interval of more than two years having elapsed since operation.

A man aged 40 caught his right hand in a circular saw which amputated the terminal phalanx of the middle finger and the terminal and half of the middle phalanx of the ring finger. He had not realized these had been cut off until someone saw his hand. Immediately after operation he was conscious of the presence of the amputated fingers. These phantoms were extremely painful, felt raw, itched, ached, and were so sore he wanted to take hold of them. The fingers became flexed powerfully and this pain was "killing." On 15 August 1940 he suddenly became unconscious and partially paralyzed on the right side. He recovered considerable function of the limbs and there was very little if any sensory deficit. There was no alteration of the phantom fingers or pain. However, he had a few convulsions after each of which the pain in the phantom disappeared for a day but recurred with its previous severity and persistence. Because of his incapacitating, unbearable pain it was decided to remove the sensory cortex corresponding to the parts amputated. This was done on 10 December 1941 under local anaesthesia. The left post-central cortex was stimulated and after determining the area corresponding to the middle and ring fingers for the right hand this was excised by subpial resection. The piece of cortex (Fig. 2) removed measured 15 by 10 by 8 mm. There was an immediate disappearance of the phantom fingers and the pain which have not recurred two years after the operation.

Thus from analysis of the clinical experiments offered by surgical therapy the unmistakable conclusion is reached that stimuli originate at the periphery in the stump with its amputated nerves which transmit these impulses by all possible pathways to registration in consciousness. Inactivation of these stimuli by novocaine block at the site of origin or by mechanical interruptions along the pathways through which they are transmitted, various

and multiple though they be, have stopped the phenomenon at the lowest level. Perception at the highest level has been altered by hypnosis.[1] Elimination of an intermediate level in this chain of sensory stations, the post-central cerebral cortex, has also silenced the ghost. Interruption of the single peripheral pathways, the lowest level, has been tedious and usually without effect because when one road was cut the impulses detoured by way of another, and if that also were blocked, still other bypaths were found. Attack on the absolute periphery of this phantom system is only temporarily effec-

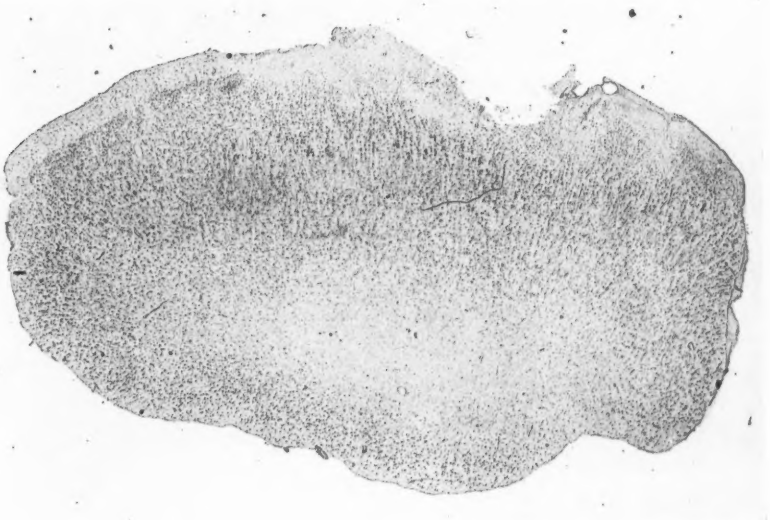


FIG. 2. Microphotograph of the section of post-central cortex removed at operation. Nissl technique (×16).

tive because excision of a neurofibroma leaves us with a pathophysiological state similar to that which followed amputation of the limb, and stimuli will start immediately or very soon at the end of the newly amputated nerve. These will become more vigorous as time allows the end of the nerve to develop another neurofibroma, the inevitable pathological process which occurs at the end of a nerve whether it is cut or injected with alcohol, formalin, or other fixatives. There is thus no permanent inhibition of the phenomenon by attack at the periphery, including interruption of the nerve anywhere in its entire extent. Because of the very numerous peripheral pathways which would have to be interrupted (anterior roots, posterior roots and sympathetic chain) it seemed preferable to eliminate the intermediate level in the sensory sequence leading to consciousness, and the post-central cortex corresponding to the phantom limb was removed. Since this stopped the phan-

tom, one may say without hesitation that for the existence of a phantom limb there must be a divided peripheral nerve stump and a sensory cortex which had been adequately mature at the time of amputation to have experienced a consciousness of the living behavior of the amputated limb.*

SUMMARY

Phantom limb is a disorder which has an organic basis—a divided peripheral nerve from which stimuli originate and are transmitted through higher levels to conscious registration. The painful phantom can be stopped by interruption of the sensory chain leading to consciousness. Since the peripheral (lower level) pathways are multiple it is simpler to interrupt the chain at the intermediate level by removal of the corresponding part of the postcentral cortex. This has been effective in a patient whose operation was done more than two years ago.

REFERENCES

1. Betlheim, S. Zur Lehre vom Phantom. *Dtsch. Z. Nervenheilk.*, 1926, *90:* 271–283.
2. Foerster, O. Über das Phantomglied. *Med. Klinik*, 1931, *27:* 497–500.
3. Foerster, O., and Gagel, O. Die Vorderseitenstrangdurchschneidung beim Menschen. Eine klinisch-patho-physiologischanatomische Studie. *Z. ges. Neurol. Psychiat.*, 1932, *138:* 1–92.
4. Foerster, O. Der Schmerz und seine operative Bekämpfung. *Nova Acta Leop. Carol.*, 1935, *3* (n.F.): 1–60.
5. Head, H., and Holmes, G. Sensory disturbances from cerebral lesions. *Brain*, 1911, *34:* 102–254.
6. Leriche, R. Les douleurs des moignons d'amputation. *Pr. méd.*, 1932, *40:* 869–873.
7. Leriche, R. La chirurgie de la douleur. *Paris: Masson et Cie.*, 1937, 428 pp.
8. Livingston, W. K. Fantom limb pain. A report of ten cases in which it was treated by injections of procaine hydrochloride near the thoracic sympathetic ganglions. *Arch. Surg., Chicago*, 1938, *37:* 353–370.
9. Mitchell, S. W. Phantom limbs. *Lippincott's Mag. pop. Lit. Sci.*, 1871, *8:* 563–569.
10. Mitchell, S. W. Injuries of nerves and their consequences. *Philadelphia: J. B. Lippincott & Co.*, 1872, 377 pp.
11. Paré, A. La maniere de traicter les playes faictes tãt par hacquebutes, que par fleches: & les accidentz d'icelles, cõme fractures & caries des os, gangrene & mortification: auec les pourtraictz des instrumentz necessaires pour leur curation. Et la methode de curer les combustions principalement faictes par la pouldre à canon. *Paris: Iean de Brie*, 1551, [8], 80, [10] *ll.*
12. Pick, A. Zur Pathologie des Bewusstseins vom eigenen Körper. Ein Beitrag aus der Kriegsmedizin. *Neurol. Zbl.*, 1915, *34:* 257–265.
13. Pitres, A. Étude sur les sensations illusoires des amputés. *Ann. méd.-psychol.*, 1897 (8e sér.), *5:* 1–19, 177–192.
14. Riddoch, G. Phantom limbs and body shape. *Brain*, 1941, *64:* 197–222.
15. Souques and Poisot. Origine périphérique des hallucinations des membres amputés. *Rev. neurol.*, 1905, *13:* 1112–1116.

* Phantom limbs are not found in patients who have had a congenital amputation or in those who have undergone amputation in infancy.

A NEUROSURGICAL HEAD REST FOR USE IN ARMY AND NAVY HOSPITALS*

CAPTAIN W. M. CRAIG (MC), U.S.N.R.
Surgical Section, U. S. Naval Hospital, Bethesda, Maryland

(Received for publication March 3, 1944)

FOR MANY YEARS it has been found advantageous to carry out certain neurosurgical operations with the patient in the sitting or upright position. In some clinics dental chairs were converted to supply this need. In others, elaborate appliances were constructed which could be attached to the operating tables, or various special tables were designed for this purpose.

Shortly after being called to active duty in the Navy, it became apparent that the hospitals connected with the Armed Services needed a simple attachment to an ordinary operating table for this purpose that was inexpensive, of relatively small size, and combined certain essential features that could be universally used by the Army as well as the Navy.

At the Naval Medical Center in Bethesda where the usual operating tables were included in the surgical equipment, such an apparatus was designed and the rough model was tried. It proved so valuable for operations on the brain and cervical portion of the spinal cord that the original apparatus was modified by the manufacturer and is now available.†

Removal of cerebellar tumors, resections of the eighth and ninth nerves for Ménière's disease and glossopharyngeal neuralgia, hemilaminectomies in the cervical region of the spinal cord and various other operations about the neck and head have been facilitated by having the patient in the upright position. The escape of blood and cerebrospinal fluid by gravity leaves the operative field clean and the exposure unobstructed. This upright or sitting position has been used almost universally for the section of the fifth cranial nerve for the relief of trigeminal neuralgia. Certain other operations on the parietal and temporal region of the head can be done in this position also with great ease.

One of the great objections to the upright or sitting position for neurosurgical operations has been the variations which occur in the blood-pressure recordings during the operation and the necessity of lowering the head of the patient in the midst of the surgical procedure. The head rest in question obviates this danger as the patient can be in the sitting position with the feet and legs elevated to the level of the head. As a further precaution it has been found that splinting the vascular bed of the lower extremities has a most profound stabilizing effect on the blood pressure. If the legs are

* The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or as reflecting the views of the Navy Department or the naval service at large.

† Manufactured by the American Sterilizer Company, Erie, Pennsylvania.

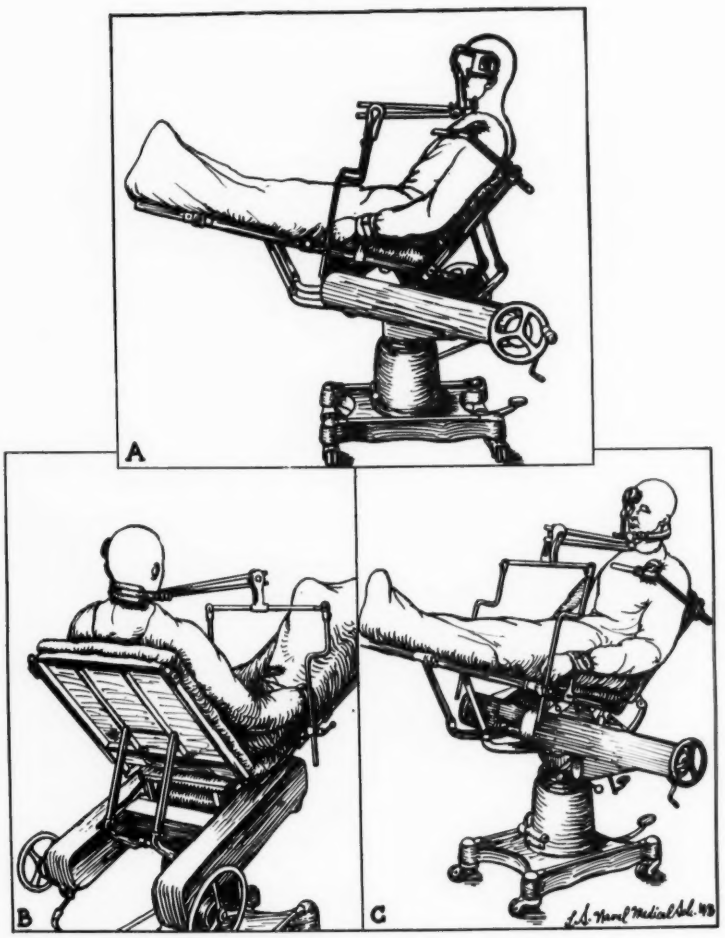


FIG. 1. *A*. Lateral view of head-rest attachment showing use of stirrup rods and shoulder supports. In this position for the posterior approach to brain and spinal cord operation the feet can be elevated and the head lowered without interruption of the operator. *B*. Posterior view with head prepared for right-sided occipital temporal and parietal operation. Patient to right of midline of table allowing for a closer approach. *C*. Antero-lateral view showing setup for a left frontal or temporal craniotomy.

wrapped in ordinary bandage of one thickness from the ankle to the groin, even when the operation is carried out under general anesthesia, the blood pressure will not vary unless there is an extraordinary loss of blood at the operation.

The head rest consists of a bar which can be attached to the stirrup rods which come as ordinary equipment of the operating table. To this bar is attached a movable and adjustable head rest in which the head can be fitted

in almost any position for suboccipital operations, ventricular drainage, and cervical laminectomies when the operation is to be done from the posterior approach. For the lateral approach the head can be adjusted so that a proper exposure of the temporal or parietal area can be obtained. The head rest has a cup-like support for the chin and straps can be used to stabilize the head. Shoulder supports have been designed to prevent the slumping of the shoulders, and with the patient in the sitting position, the feet and legs elevated, there is no tendency for the patient to slip down.

The entire apparatus is so constructed that the patient can be in the center of the table for posterior approaches, or can be placed to the right or left of the midline for temporal or parietal operations. Nearly all of the tables used for operations carried out in the upright position necessitate the legs and feet to be held in the dependent position and create a postural blood-pressure problem. This tendency was overcome by wrapping the legs from ankle to groin with bandage before placing the patient in the upright position. The use of an ordinary operating table with the new head rest attached, allows the patient to sit up without having the legs dependent. In fact, the table can be so adjusted that the feet are maintained at the same level as the head, and the additional precaution of wrapping the legs allows for two safeguards against postural anesthetic hypotension.

The benefits of this particular type of head rest consist in its simple attachment to the ordinary operating table in use in the Army and Navy Hospitals, its convenient size enabling it to be stowed away when not in use, and its mobility so that it can be transported easily. The neurological surgeon in the Armed Services is furnished with a convenient portable head rest which can be attached to the ordinary operating table providing him with the necessary equipment to carry out operations upon the brain and spinal cord in the upright or sitting position.

TRAUMATIC PNEUMOCEPHALUS WITH SPONTANEOUS VENTRICULOGRAMS

REPORT OF A CASE*

COMDR. ABRAHAM KAPLAN (MC), U.S.N.R.
Surgical Service, U. S. Naval Hospital, Newport, Rhode Island

(Received for publication March 10, 1944)

TRAUMATIC pneumocephalus, though still rare, is now being recognized with increasing frequency. In 1884 Chiari[8] was the first to demonstrate at post mortem that air had entered the frontal lobe and ventricular system through a rent communicating with the ethmoidal cells. It was not until 1913 that Luckett[15] first reported X-Ray evidence of air in the ventricles of the brain following a skull fracture. Since then similar reports have been more frequent and in 1926 Dandy[11] collected 25 cases and added 3 of his own. Nevertheless further discussion of this condition may be of interest.

Cerebrospinal rhinorrhea with pneumocephalus may be due to various causes. It may occur spontaneously in a patient with congenital arachnoidal prolongations along the olfactory nerve after a severe sneezing spell.[12] Most often, however, pneumocephalus is secondary to a fracture of the skull involving the posterior wall of the frontal sinus or cribriform plate of the ethmoid bone. As the bone is fractured there is an accompanying tear of the dura which may extend through and communicate with the arachnoid, brain substance or ventricles, thereby establishing a sinus through which there is an exchange of fluid and air. The air may then be trapped in the subdural, subarachnoid, or ventricular spaces. Air may even pocket itself within the brain substance. Not infrequently the dural tear and sinus tract may be so small as to escape detection at operation. Coleman[9] states that cerebrospinal rhinorrhea occurs in about 2 to 5 per cent of skull fractures. Other and more unusual causes of cerebrospinal rhinorrhea and pneumocephalus are intranasal manipulation,[5] chronic infection in the region of the cribriform plate,[8,13,14] erosion into the anterior cranial fossa by an orbito-ethmoidal osteoma,[7,10] downward extension of a pituitary neoplasm through the sphenoidal sinus,[16] and craniotomy.

Meningitis is, of course, the greatly feared complication of cerebrospinal rhinorrhea and in untreated cases the mortality varies from 40 to 50 per cent.[3,4,11] However, with the use of sulfonamide drugs the outlook today is more favorable. Measures including rest, dependent posture, and a decrease in intracranial pressure favor the stoppage of cerebrospinal rhinorrhea and may be followed by a spontaneous cure. Adson,[1] Cairns,[6] Coleman[9] and Dandy[11] advocate surgical repair of the meninges if rhinorrhea does not dis-

* This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth are those of the writer and are not to be construed as reflecting the policies of the Navy Department.

appear within 4 to 6 days after the injury. Surgical intervention in properly selected cases, adequately prepared with sulfonamide drugs, carries a minimal risk. In a recent report by Adson[2] there were no deaths in eight consecutive cases treated surgically.

The following case is reported because of the unusual delayed appearance of cerebrospinal rhinorrhea, and the unusual X-Ray findings.

F.J.L. a 30 year old Q.M. 2/c, was admitted to the Naval Hospital in a critical condition 26 days after a serious automobile accident. At daybreak on July 3, 1943 he had fallen asleep at the wheel of his automobile, veered to the left, and collided head-on with an automobile traveling in the opposite direction. He was brought to a nearby hospital in a desperate condition of shock. After the administration of intravenous fluids and intramuscular injections of coramine, adrenal cortex and thiamine hydrochloride his condition improved. Examination, which was necessarily incomplete, showed a depressed fracture of the right frontal bone involving the orbital margin, multiple fractures of the lower jaw and a comminuted fracture of the left femur. A Kirschner wire was put through the lower end of the femur and the leg put in a Thomas splint. Urine showed a few red blood cells only upon first examination. From the day of the accident until July 27, 1943 he was very restless, noisy, and at times maniacal. The temperature varied from 99 to 101. Abscesses under the chin which developed at the sites of fracture of the mandible were incised. He was given paraldehyde and bromides for restlessness, 50 mg. of ascorbic acid twice a day, as well as daily intravenous fluids. On July 27, 1943 his condition permitted his transfer to a nearby Naval Hospital and after two days' observation there he was transferred to this hospital.

Examination. He was a critically ill, dehydrated young man who could hardly be aroused and who, most of the time, was uncommunicative. At times he was very irritable and abusive. There was a conspicuous depression and deformity involving the right frontal bone and orbit. The lower jaw was so swollen and inflamed that the mouth could hardly be opened. The alignment of the teeth was seriously disorganized. Under each submental region there was a draining sinus from which pus could readily be expressed. The left femur was fractured at the midshaft with two inches overriding. Except for impaired bilateral grasp reflex, neurological examination was essentially negative. Temperature was 97, pulse 80 per minute, and blood pressure 130 systolic, 80 diastolic. Urine was negative. Hgb. 75 per cent; red blood cells 4,560,000 per c. mm., leucocytes 16,000 per c. mm. with 86 per cent polymorphonuclear cells, and 14 per cent lymphocytes.

Course. The patient was placed on a regime of intravenous fluids, warm irrigations of the mouth with potassium permanganate, and local wet dressings for the abscesses. Within 24 hours he was able to take small quantities of fluids by mouth, and sulfathiazole (15 gr.) was administered orally every 4 hours without interruption. After two days of this supportive regime the patient's general condition improved sufficiently for X-Ray examination.

Roentgenograms. Films of the skull showed a compound depressed comminuted fracture of the right frontal bone through the frontal sinus and cribriform plate with pneumoventriculogram showing asymmetrical dilatation of the lateral ventricles and striking cortical atrophy (Fig. 1). The lateral film, with the patient in supine position, and the X-Ray beam horizontal, showed distinct fluid levels (Fig. 2). The pineal shadow was not displaced. X-Ray films of the mandible showed an oblique fracture through the left condyle, and compound fractures in the left molar and right cuspid regions, with several sequestrae.

Because of the surprising and unusual finding of pneumoventriculograms further studies of the skull were arranged for the following day. It was then, while the patient was being turned in the prone position, that clear fluid began to escape from the right nostril. About 5 cc. of this fluid was collected which showed 22 cells per c. mm., but no organisms on smear or subsequent growth. X-Ray films of the skull taken at this time showed a well outlined ventricular system with only slight dilatation of the right anterior horn (Figs. 3 and 4). The cerebrospinal rhinorrhea continued.

Operation. Craniotomy was performed on August 3, 1943, under intratracheal ether (Lt. George J. Matusak (MC), U.S.N.R., anaesthetist), supplemented with local novocaine for the scalp. The right frontal bone was exposed after reflecting the scalp by a curved incision within the hairline. A loose triangular fragment of the frontal bone had to be sacrificed, and in so doing the right frontal sinus was exposed. The depressed frontal bone was then elevated and the fractured orbital ridge brought into alignment. The mucous membrane of the exposed frontal sinus was removed. The dura appeared normal in color, and pulsated freely. Bleeding

FIG. 1 (*left*). Roentgenogram showing compound fracture of right frontal bone involving frontal sinus and cribriform plate. Note asymmetrical dilatation of both lateral ventricles without displacement and air in right temporal horn. Note also fractures of mandible.

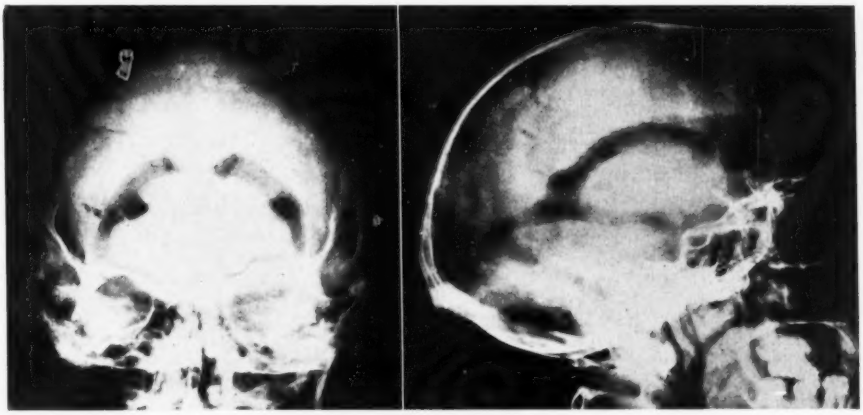
FIG. 2 (*right*). Side view showing fluid levels in both frontal and right temporal horns.

from the orbital ridge was controlled with bone wax. The right frontal lobe was elevated exposing the cribriform plate where a linear fracture was visualized to the right of the crista galli. The dura was carefully inspected but no defect could be found. A stamp of fascia taken from the temporal region was placed over the site of fracture. Two silver clips were attached to the fascial stamp to mark the location of the plastic repair. After careful hemostasis, sulfanilamide powder was dusted into the wound and closure was carried out in layers using silk throughout.

Postoperative Course. Convalescence was smooth. On the day after operation the cerebrospinal rhinorrhea ceased and has not recurred since. The wound healed by primary union. Sulfathiazole (15 gr. daily) was continued orally for a fortnight.

The patient became progressively more alert, calmer, and more responsive to questioning. One could observe almost daily mental improvement. Neurological examination showed only bilateral anosmia.

Roentgen films of the skull taken one week after operation showed a triangular bony operative defect over the right frontal region and two small metallic bodies in the region of the cribriform plate. The depressed frontal bone had been elevated (Fig. 5). The air seen in



FIGS. 3 and 4. Spontaneous ventriculograms showing size and shape of lateral and third ventricles. Note slight dilatation of right frontal horn.

previous skull films was no longer present. X-rays of the fractured left femur held in position with Kirschner pin traction showed satisfactory alignment and healing with good callus formation. Following the removal of sequestrae at the site of the mandibular fractures, Winter's arch splints were applied. The mandible then healed without further difficulty.

At present the patient's mentality, personality and behavior have returned to his previous normal state. Except for bilateral anosmia, neurological examination is negative. There are no subjective complaints of headache, dizziness or visual disturbance. The only residual

FIG. 5 (*left*). Postoperative view after elevation of depressed fracture. Note silver clips at the site of plastic repair over the cribriform plate.

FIG. 6 (*right*). Patient at time of discharge.

is a minimal asymmetry of the eyes and forehead (Fig. 6). On February 11, 1944 the patient was returned to duty.

REFERENCES

1. Adson, A. W. Cerebrospinal rhinorrhea; surgical repair of fistula: report of a case. *Proc. Mayo Clin.*, 1941, *16:* 384–387.
2. Adson, A. W. Results following surgical repair of craniosinus fistula for cerebrospinal rhinorrhea: abstract of a published paper with comment on subsequent experience. *Proc. Mayo Clin.*, 1942, *17:* 281–286.
3. Baker, G. S., and MacLean, A. R. Cerebrospinal rhinorrhea associated with pneumocephaly, pneumococcic meningitis and abscess of the brain: report of a case. *Proc. Mayo Clin.*, 1941, *16:* 746–750.
4. Barden, R. P. Traumatic pneumocranium. A report of two cases. *Amer. J. Roentgenol.*, 1940, *43:* 514–516.
5. Bulson, A. E., and Bulson, E. L. Cerebrospinal rhinorrhea following intranasal surgery. *J. Amer. med. Ass.*, 1929, *93:* 1969–1971.
6. Cairns, H. Injuries of the frontal and ethmoidal sinuses with special reference to cerebrospinal rhinorrhoea and aeroceles. *J. Laryng. Otol., Edinb.*, 1937, *52:* 589–623.
7. Campbell, E. H., and Gottschalk, R. B. Osteoma of frontal sinus and penetration of lateral ventricle, with intermittent pneumocephalus. *J. Amer. med. Ass.*, 1938, *111:* 239–241.
8. Chiari, H. Ueber einen Fall von Luftansammlung in den Ventrikeln des menschlichen Gehirns. *Z. Heilk., Prag.*, 1884, *5:* 383–390.
9. Coleman, C. C. Fracture of the skull involving the paranasal sinuses and mastoids. *J. Amer. med. Ass.*, 1937, *109:* 1613–1615.
10. Cushing, H. Experiences with orbito-ethmoidal osteomata having intracranial complications. With the report of four cases. *Surg. Gynec. Obstet.*, 1927, *44:* 721–742.
11. Dandy, W. E. Pneumocephalus (intracranial pneumatocele or aerocele). *Arch. Surg., Chicago*, 1926, *12:* 949–982.
12. Friedberg, S. A., and Galloway, T. C. Spontaneous cerebrospinal rhinorrhea. *Ann. Otol. etc., St. Louis*, 1938, *47:* 792–794.
13. Johnston, W. H. Cerebrospinal rhinorrhea—the study of one case and reports of twenty others collected from the literature published since nineteen hundred. *Ann. Otol. etc., St. Louis*, 1926, *35:* 1205–1240.
14. Learmonth, J. R. Cerebrospinal rhinorrhea treated by operation. *Proc. Mayo Clin.*, 1929, *4:* 115–116.
15. Luckett, W. H. Air in the ventricles of the brain, following a fracture of the skull. Report of a case. *Surg. Gynec. Obstet.*, 1913, *17:* 237–240.
16. Smith, C., and Walter, L. Cerebrospinal rhinorrhea with cyst of the pituitary body. Treatment and apparent cure: report of a case. *Arch. Otolaryng., Chicago*, 1931, *14:* 610–614.

STUDIES ON FIBRIN FOAM AS A HEMOSTATIC AGENT IN NEUROSURGERY, WITH SPECIAL REFERENCE TO ITS COMPARISON WITH MUSCLE*

FRANC D. INGRAHAM, M.D., ORVILLE T. BAILEY, M.D., AND FRANK E. NULSEN, M.D.

Departments of Surgery and Pathology, Harvard Medical School, and the Surgical Services of the Peter Bent Brigham and The Children's Hospitals, Boston, Massachusetts

(Received for publication March 31, 1944)

THE PROMPT and complete control of bleeding with the minimum of injury to living tissue is of first importance in all forms of surgery. Perfect hemostasis is especially difficult in many neurosurgical procedures and the securing of it occupies a considerable portion of the time required by these operations. The various agents in current use for this purpose have been considered elsewhere.[1,2] A completely satisfactory hemostatic material for neurosurgical procedures should meet several criteria. It should be readily available; it should produce prompt control of bleeding; it should result in no (or very slight) tissue reaction; it should not cause the formation of antibodies.

In the course of fractionation of human blood plasma[3] large quantities of human fibrinogen and thrombin have become available. Bering[4] has prepared from these materials a substance designated "fibrin foam." The product is composed of a porous mass of fibrillar fibrin with macroscopic air spaces. When the foam is moistened, fluid rapidly enters the air spaces. It then becomes rubbery and shrinks to a certain extent. If the moistening agent is a solution of human thrombin, the foam becomes an effective hemostatic agent. While the fibrin foam and thrombin may be used in many forms of surgery, our experiences are limited to neurosurgery. In this field, it has proved the most satisfactory hemostatic agent available.[2,4]

For use in the operating room, two bottles are provided. One contains sterile fibrin foam and the other thrombin in the dry state. The thrombin is dissolved in 30 cc. of sterile physiological saline solution. Pieces of the fibrin foam are then placed in the thrombin solution, after which the material is ready for use. For application to bleeding surfaces, a piece of appropriate size is cut and held firmly against the tissue. This is usually best accomplished by covering it with a cotton pattie and applying suction for a moment. When

* This work has been carried out under contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University.

This paper is No. 28 in the series "Studies on Plasma Proteins" from the Harvard Medical School, Boston, Massachusetts, on products developed in the Department of Physical Chemistry from blood collected by the American Red Cross.

the pattie is removed, the fibrin foam remains adherent to the tissue surface.

It is the purpose of this paper to describe additional experiments with fibrin foam and to record further clinical experiences with the material as a hemostatic agent in neurosurgery. The experiments have been designed to test further the safety of the material and to compare its behavior with that of other hemostatic agents in neurosurgery, especially muscle.

THROMBIN IN THE SUBARACHNOID SPACE

In the application of fibrin foam soaked in thrombin solution to various parts of the central nervous system, it is probable that at times an excess of thrombin solution enters the subarachnoid space and from thence it may be disseminated by the cerebrospinal fluid. The concentration of thrombin thus circulated would of necessity be small unless the foam were applied with gross carelessness. It seemed advisable, however, to determine experimentally whether the thrombin prepared by the fractionation of human plasma would set up inflammatory or other undesirable reactions in the meninges when introduced into the subarachnoid space.

Three monkeys (*Macaca mulatta*) were used as test animals. In each monkey a lumbar puncture was performed under nembutal anaesthesia. Two cc. of cerebrospinal fluid were withdrawn and replaced by 2 cc. of a saturated solution of human thrombin. One monkey was sacrificed after 3 hours, another after 24 hours, and the third after 6 days. During the period of observation, no physiological abnormalities appeared. The spinal cords and brains were then removed and fixed in 10 per cent formalin. After hardening, numerous blocks were selected so as to include many levels of the spinal cord both near to and remote from the site of injection, as well as various areas of the brain. These blocks were embedded in paraffin and sections stained with hematoxylin and eosin.

The sections of the monkey sacrificed after three hours were entirely normal except for one minute area in the meninges over the pons where a small number of polymorphonuclear leucocytes were found. In the monkey sacrificed after 24 hours there were two small foci of polymorphonuclear leucocytic infiltration, one in the meninges over the cerebral cortex and the other in the meninges of the cerebellum. All other sections of the brain and spinal cord showed no evidence of change. The sections of the monkey sacrificed six days after the injection of the thrombin showed as their only abnormality a minute collection of lymphocytes with a very few eosinophiles in the meninges overlying the cornu Ammonis. Again, all levels of the spinal cord were free from inflammatory reaction or other alterations.

The changes which have been described were so slight as to make their significance doubtful. They seem best interpreted, however, as indicating that a very mild reaction in the subarachnoid space may be set up by a relatively large amount of thrombin. At most, the reaction is very much less than that occasioned by an equal volume of blood injected in the same manner. In all three animals, the sections of the spinal cord, including those at the site of injection, were entirely normal. This should tend to indicate that the thrombin is rapidly dispersed by the circulation of the cerebrospinal fluid.

Before the development of fibrin foam, severe bleeding was treated with thrombin alone in a small group of patients. In one of these the lateral ventricle was entered in relieving a ventricular block caused by a huge glioblastoma multiforme of the left cerebrum, which occluded the left foramen of

Monro. An incision was made through the tumor and enough neoplastic tissue was removed to restore the circulation of cerebrospinal fluid. Free bleeding resulted. In order to control this, thrombin solution was applied, and during the procedure a considerable amount of the solution escaped into the ventricular system. No evidence was detected clinically that there were ill effects from the thrombin in the cerebrospinal fluid.

From these data, it appears that the escape of even a considerable amount of thrombin into the cerebrospinal fluid is not attended by a reaction sufficient to be of clinical moment.

COMPARISON OF FIBRIN FOAM AND MUSCLE AS HEMOSTATIC AGENTS

The introduction of muscle as a hemostatic agent in 1911 by Cushing[5] was a definite advance in neurosurgery. Muscle has proved of great value in controlling ooze from vessels unsuited to ligation and is often very useful in dealing with bleeding from the dural sinuses and other large venous channels. Its greatest value lies in the fact that it is absorbed and therefore may be left in place at the end of operation. Similar types of bleeding are often well controlled with moist cotton but in many instances the removal of the pattie may pull away the clot and the bleeding then begins anew.

Fibrin foam soaked in thrombin is another absorbable hemostatic material for use in situations similar to those in which muscle has for long been the agent of choice. Muscle, as used in the operating room, is of human origin and is usually autogenous. Fibrin foam and thrombin are both prepared entirely from human blood plasma and thus share with muscle the advantage accruing from the use of material of human origin.

A very important consideration in making a choice between muscle and fibrin foam with thrombin as a hemostatic agent is the tissue reaction caused by each. The tissue reaction to muscle has been studied by Harvey[6] and others. However, it seemed advantageous to make a direct comparison between the responses excited by muscle and those excited by fibrin foam with thrombin by testing both materials in the same animal.

An identical experimental procedure was carried out in six monkeys (*Macaca mulatta*). Each was anaesthetized with nembutal and the scalp shaved. Bilateral temporal craniotomies were performed and the cerebral cortex exposed by opening the dura. A piece of the monkey's temporal muscle, approximately 4×4×5 mm. in size, was placed within the substance of the right parietal lobe through a small cortical incision. In a similar manner, a piece of fibrin foam soaked in thrombin of the same size as the muscle fragment was placed within the cortex of the left parietal lobe. The dura was then closed on both sides and the scalp tightly sutured. One monkey was sacrificed with an overdose of nembutal at the following intervals after operation: 3 days, one week, 2 weeks, 19 days, 3 weeks and 4 weeks. No physiological abnormalities developed during the period of observation. When the animals were sacrificed, the heads were removed. The skin, jaws and other excess tissue were then dissected away and the skull with its contents fixed in 10 per cent formalin. After fixation, the bone was removed without opening the dura. Gross observations were made and numerous blocks of dura and cerebral cortex were selected. The blocks were embedded in paraffin and sections stained with hematoxylin and eosin.

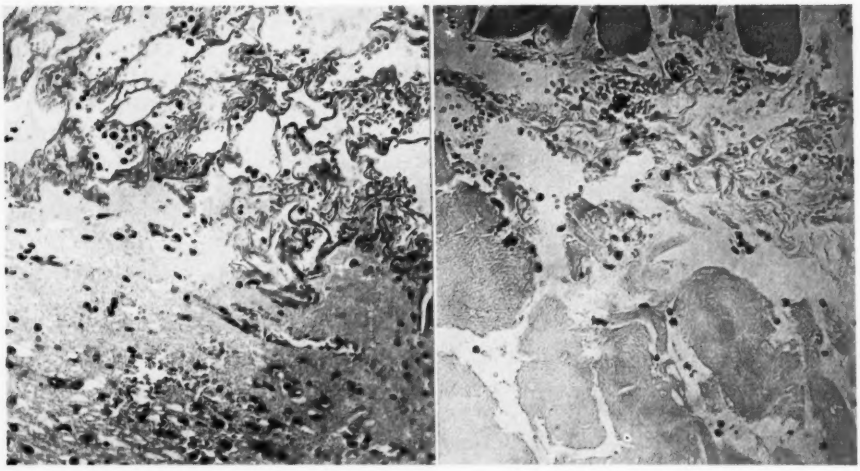


FIG. 1 (*left*). Tissue reaction to fibrin foam 19 days after operation. Note the mild cellular infiltration and the remnants of fibrin foam within the brain substance.

FIG. 2 (*right*). Center of the fragments of muscle 19 days after implantation. The muscle fibers are still clearly visible and there is a mild infiltration of this portion of the fragment.

In the monkey sacrificed 3 days after operation, both fibrin foam and muscle were present. About the foam there were a few mononuclear cells and rare polymorphonuclear leucocytes. No giant cells were seen. A few bits of foam in the subdural space caused very little reaction. The general morphology of the muscle fibers was quite well preserved, though they took a paler stain than does normal fresh muscle. Polymorphonuclear leucocytes were found in considerable numbers at the periphery and occasional cells of this type were scattered through the interior of the muscle fragment.

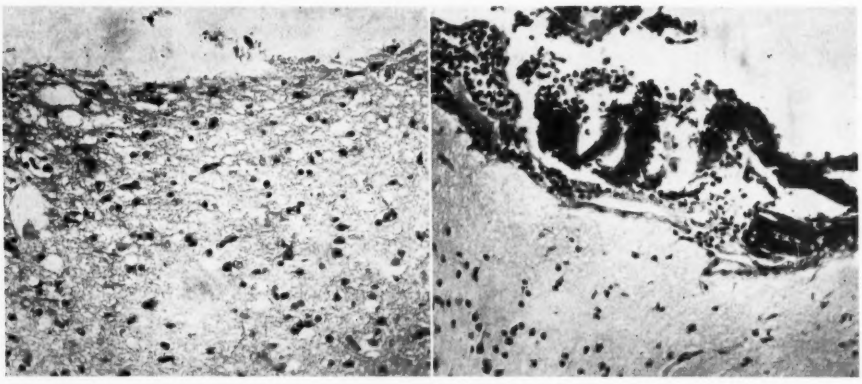


FIG. 3 (*left*). Glial reaction about muscle implanted in the cerebral cortex 9 days previously.

FIG. 4 (*right*). Polymorphonuclear leucocytic reaction to bits of muscle extruded on to the meningeal surface.

After one week, there were a few mononuclear cells about the foam, the polymorphonuclear reaction being even less than at 3 days. Polymorphonuclear leucocytes were present, however, about the muscle and there was proliferation of fibrous tissue.

At 2 weeks, 19 days and 3 weeks, there were occasional polymorphonuclear leucocytes and mononuclear cells within the foam. Glial reaction was minimal and fibrous tissue reaction hardly detectable (Fig. 1). On the other hand, the polymorphonuclear leucocytic reaction in the muscle implant was more extensive (Fig. 2) and there was about it a zone of gliosis with some fibrous tissue proliferation (Fig. 3). Bits of the muscle implant had been extruded into the subdural space and these were surrounded by large numbers of polymorphonuclear leucocytes (Fig. 4).

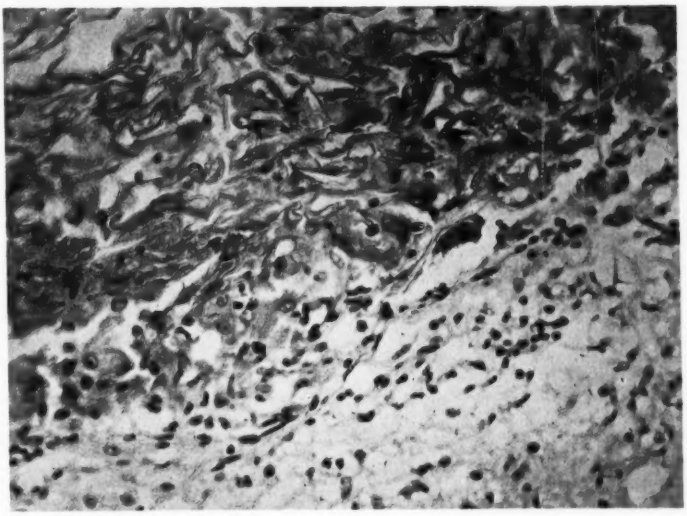


FIG. 5. Residual foam 4 weeks after implantation in the cerebral cortex.

In the monkey sacrificed 4 weeks after operation, only a small amount of foam remained. This was surrounded by a few lymphocytes and at the periphery giant cells had formed about the foam. Gliosis was very slight and fibrous tissue reaction was almost wholly lacking (Fig. 5). The meninges were normal. A much larger amount of muscle was still present. This was becoming transformed into fibrous tissue (Fig. 6) and was calcified in places (Fig. 7). Mononuclear cells were present in relatively small numbers. Considerable reactive gliosis was present about the fragment. Bits of muscle extruded into the subdural space were adherent to the dura and were surrounded by considerable amounts of fibrous connective tissue (Fig. 8).

These experiments indicate clearly that the tissue reaction due to fibrin foam with thrombin is very slight. The tissue reaction to muscle is greater and, furthermore, the presence of muscle excites a considerable amount of fibrous tissue proliferation. Because of the evidence that contraction of such cicatrices may produce widespread effects on the vaso-astral framework of the brain,[7] this characteristic of tissue reaction to muscle would seem to be particularly undesirable.

Besides exciting less tissue reaction, fibrin foam with thrombin has several other characteristics which make it superior to muscle as a hemostatic agent in neurosurgery. Human fibrin foam with thrombin is manufactured

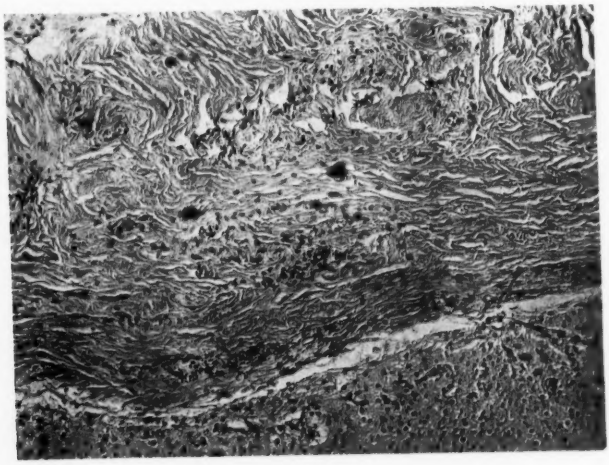


FIG. 6. Muscle 4 weeks after implantation in the cerebral cortex. The muscle is being transformed into fibrous tissue.

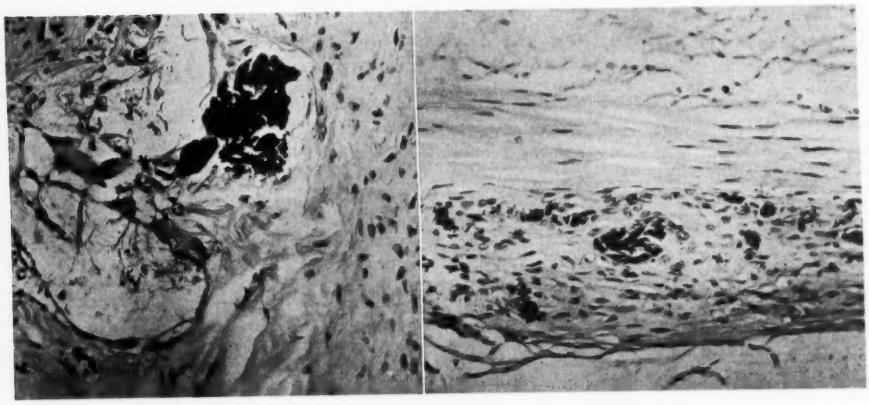


FIG. 7 (*left*). Calcification in muscle fragment 4 weeks after implantation.
FIG. 8 (*right*). Reaction to muscle which was extruded in the subdural space 4 weeks after implantation of the original fragment. Note the fibrous tissue reaction.

in amounts equal to the demand. The quantity of hemostatic material required for an operation may be placed on the sterile field as routinely as suture material. Should additional material be required for an unexpected emergency in the course of the procedure, a supply may be made ready for use at a moment's notice.

When muscle is used as a hemostatic agent, it is more difficult to be sure that an adequate amount of material is immediately available. The temporal muscle provides only a rather small supply. Recourse must then be taken to muscle from concomitant operations on other patients, but such may not be going on in an adjoining operating room. It is then necessary to perform a separate procedure to secure muscle, usually from the gastrocnemius. This is obviously undesirable. Muscle from laboratory animals has been used by a few neurosurgeons. Because of the possibility of sensitizing the patient to the proteins of the animal this has definite limitations and the use of heterologous muscle might be attended with more severe reaction when used at a second operation.

Fibrin foam can be broken or cut to the size required for a given bleeding surface far more easily than can muscle. At the same time, an excess of fibrin foam will do no harm because of the slight tissue reaction to it, while there is sufficient tissue response to muscle to make it important that no excess be used. We have found it technically advantageous to place a very large amount of fibrin foam with thrombin in tumor beds and other extensive bleeding surfaces and then pull out the central portion. This can be done with no fear of dislodging the fibrin foam in contact with the tumor bed and a coating of hemostatic material thus remains in place. While it might not cause any significant reaction to leave a piece of fibrin foam the size of a golf ball, it is usually unnecessary. It would appear disadvantageous to replace a neoplasm with a mass of fibrin foam of equal dimensions.

Another desirable characteristic of the fibrin foam is that it can be moulded to a certain extent and holds the shape into which it is pressed. This is called "permanent set." Not only can this be done before the fibrin foam has been put in place but it can also be further molded *in situ*. The fibrin foam thus accepts the conformation of the bleeding surface when it is applied and retains this conformation. Muscle, on the other hand, can be cut to conform in general to the surface but it cannot be moulded or made to conform to the particular contours of the special bleeding surface under consideration. The tissue structure of muscle prevents it from having the adaptability of fibrin foam in these respects.

In one patient, fibrin foam has been applied to the choroid plexus, which had been exposed through a transcortical incision. This procedure led to no difficulty that could be detected clinically. Should the fibrin foam become free in the ventricular system, it would be absorbed with minimal tissue reaction, but this would be unlikely in view of the firm adherence of the fibrin foam. It would be hazardous to use muscle on the choroid plexus because it might easily become dislodged and occlude the aqueduct. This is a clinical impression and has not been tested in experimental animals.

Muscle as a hemostatic agent has in general been reserved by neurosurgeons for emergency situations where the other methods of hemostasis have failed. Such emergencies are cared for at least as well by fibrin foam with thrombin. These two agents control bleeding from the dural sinus or blood vessel malformations equally well. However, a rather large plaque of either

is required. Under these circumstances, the slight tissue reaction due to the fibrin foam makes it preferable to muscle. Fibrin foam with thrombin is more satisfactory than muscle for controlling bleeding from the large cerebral veins entering the superior longitudinal sinus because it can be moulded before and after application. Fibrin foam with thrombin thus is significantly superior to muscle in the situations in which muscle has been the most useful.

Fibrin foam with thrombin has been employed in places where neurosurgeons have seldom used muscle. It is our impression that small oozing points, as in laminectomies or in some tumor beds, can be very rapidly controlled by the use of fibrin foam with thrombin. Such bleeding is stopped satisfactorily with hot saline patties and pressure, but the procedure takes considerable time. As much as a half hour or even an hour may be saved in many operations by the use of fibrin foam with thrombin for the immediate control of oozing from small bleeding points. Hemostasis secured with this material is as complete, or more so, as that obtained by the conventional methods. Such considerable saving of time is valuable to civilian patients and also might make it possible for a neurosurgeon in the armed forces to deal with more patients per day when that is a prime consideration.

For these reasons, fibrin foam with thrombin is definitely superior to muscle as a hemostatic agent in neurosurgery. It is effective in all the situations where muscle is now used and it excites less tissue reaction. It is useful in many situations where muscle is not used.

COMPARISON OF THE TISSUE REACTION TO FIBRIN FOAM WITH THAT OF SUTURES AND BONE WAX

While fibrin foam has been used only as a hemostatic agent, it seems desirable to compare the extent of its tissue reaction with that resulting from the use of other materials routinely employed in neurosurgery. These materials have been long recognized as safe in quantities as large as are required. If new agents cause similar or less response on the part of tissues, there is little to fear from the standpoint of tissue reaction.

Our experience with the response of tissues to sutures is confined to those of black silk. Black silk sutures cause a mild infiltration of polymorphonuclear leucocytes and mononuclear cells with later formation of giant cells and eventual encapsulation by fibrous tissue. The extent of the fibrous tissue proliferation in response to a single black silk suture is in excess of that caused by a large amount of fibrin foam.

The tissue reaction to bone wax led to the formation of considerable numbers of giant cells. There was a moderate infiltration of polymorphonuclear leucocytes and mononuclear cells. The healing process involved proliferation of connective tissue. There was a considerably greater tissue response to bone wax than to black silk sutures and very much more than to fibrin foam. Since bone wax was often used on the skulls of the monkeys reported in this paper and elsewhere,[1,2,4] it was often possible to compare the tissue reaction to

fibrin foam on the inner surface of the dura with that to bone wax on the outer surface and to black silk sutures used to close the dura. It was usually difficult to locate the site where fibrin foam had been placed, while the reactions to suture material and bone wax were obvious on even casual inspection. Since the tissue responses to black silk and bone wax have not been regarded as serious, those to fibrin foam must be considered as of still less importance.

COMPARISON OF FIBRIN FOAM AND SOLUBLE CELLULOSE IN NEUROSURGERY

Frantz[8] showed that soluble cellulose may be left in the tissues with minimal reaction. This material was prepared by the oxidation of cotton or paper by nitrous oxide.[9,10] Putnam[11] demonstrated that an excellent hemostatic material could be prepared by saturating soluble cellulose (oxidized cotton) with thrombin. He reported good results in a small number of neurosurgical operations. The material was, therefore, designed for the same purpose as fibrin foam and, like it, was soaked in thrombin solution before it became hemostatic.

Soluble cellulose is not prepared from human materials, as is fibrin foam. How much difference this may make has not been established as yet. Our studies on the relative tissue reactions elicited by these substances have been described elsewhere.[2,4] It was found that there was no essential difference in the reactions elicited by the two types of material. Either is safe in that respect.

Our experience suggests that fibrin foam has certain advantages over soluble cellulose in clinical neurosurgery. The hemostatic action of fibrin foam seems to depend not only upon the presence of the thrombin solution but also upon the manner in which it is held in the fibrin. The honeycomb structure of the fibrin foam seems better adapted to hold the thrombin in such manner as to make it an effective hemostatic agent than does the looser fibrillar structure of soluble cellulose. Support for this clinical impression is found in the demonstration that fibrin foam is an effective hemostatic agent when used with weak solutions of thrombin while soluble cellulose is not hemostatic with thrombin solutions of the same concentration.[1]

In the form supplied to us, soluble cellulose is not so readily broken up into fragments or cut to appropriate size as is fibrin foam. It is very advantageous to have the fibrin foam readily cut into discs, pellets or other shapes so that it may be readily applicable to the individual characteristics of the bleeding point at hand. Furthermore, the "permanent set" of the fibrin foam makes it retain the contours of the bleeding surface.

Another desirable property of the fibrin foam is that it adheres immediately and permanently to the bleeding surface. Soluble cellulose is less adherent and its edges tend to curl away from the surface to which it is applied. In locations where it is possible to tuck the soluble cellulose under another surface, as at the edge of the dura, this characteristic presents little diffi-

culty but on exposed surfaces the firm adherence of the fibrin foam is highly desirable. The large majority of places in which a hemostatic agent is necessary do not permit holding the material in place by methods other than its own adherence.

COMMENT

Fibrin foam with thrombin has proved a most effective hemostatic agent under a wide variety of circumstances. We have now used it in 158 operations on 113 patients. Our results have been confirmed by trials in several other clinics.

The additional experience gained since a previous report[2] has indicated a still greater number of uses for the material which have been discussed in other sections of this paper. Considerable data have also been obtained to indicate the safety of repeated use of fibrin foam in successive operations on the same patient. Multiple applications have now been made in the following number of patients:

Two applications	24
Three applications	9
Four applications	1
Total	34

No clinical symptoms referable to the multiple applications of fibrin foam developed in any of the 34 patients, and there was no evidence of additional tissue reaction or other unfavorable changes when the operative field was reexplored.

Fibrin foam has been recovered at reexploration or at autopsy and its tissue reaction in man compared with that in experimental animals. The additional material of this character obtained since previous reports[2] confirm the findings described in them. They indicate that the tissue reaction to fibrin foam in man is similar to that in experimental animals and is slight in all instances.

SUMMARY

Fibrin foam with thrombin is a readily available hemostatic agent prepared wholly from materials of human origin. It promptly controls bleeding from oozing surfaces, from large veins, and from the dural sinuses.

Muscle as a hemostatic agent is less adaptable than fibrin foam and causes considerably more tissue reaction.

Fibrin foam has several advantages over soluble cellulose, though the tissue reaction to each is similar.

Fibrin foam has been applied at more than one operation in 34 patients without change in tissue response or other damage.

The usefulness of fibrin foam is enhanced by the fact that it may be moulded to the contour of the bleeding surface before or after application, that it retains that contour after pressure is released, and that it adheres quickly and permanently to the bleeding surface.

REFERENCES

1. Bering, E. A., Jr. Chemical, clinical and immunological studies on the products of human plasma fractionation. XXII. The development of fibrin foam as a hemostatic agent and for use in conjunction with human thrombin. *J. clin. Invest.* (in press).
2. Ingraham, F. D., and Bailey, O. T. The use of products prepared from human fibrinogen and human thrombin in neurosurgery. Fibrin foams as hemostatic agents; fibrin films in repair of dural defects and in prevention of meningocerebral adhesions. *J. Neurosurg.*, 1944, *1:* 23–39.
3. Cohn, E. J., Oncley, J. L., Strong, L. E., Hughes, W. L., Jr., and Armstrong, S. H., Jr. Chemical, clinical and immunological studies on the products of human plasma fractionation. I. The characterization of the protein fractions of human plasma. *J. clin. Invest.* (in press).
4. Bailey, O. T., and Ingraham, F. D. Chemical, clinical and immunological studies on the products of human plasma fractionation. XXIII. The use of fibrin foam as a hemostatic agent in neurosurgery: clinical and pathological studies. *J. clin. Invest.* (in press).
5. Cushing, H. The control of bleeding in operations for brain tumors. With the description of silver "clips" for the occlusion of vessels inaccessible to the ligature. *Ann. Surg.*, 1911, *54:* 1–19.
6. Harvey, S. C. Fibrin paper as an haemostatic agent. *Ann. Surg.*, 1918, *68:* 66–70.
7. Foerster, O., and Penfield, W. The structural basis of traumatic epilepsy and results of radical operation. *Brain*, 1930, *53:* 99–119.
8. Frantz, V. K. Absorbable cotton, paper and gauze (oxidized cellulose). *Ann. Surg.*, 1943, *118:* 116–126.
9. Unruh, C. C., and Kenyon, W. O. Investigation of the properties of cellulose oxidized by nitrogen dioxide. *J. Amer. chem. Soc.*, 1942, *64:* 127–131.
10. Yackel, E. C., and Kenyon, W. O. The oxidation of cellulose by nitrogen dioxide. *J. Amer. chem. Soc.*, 1942, *64:* 121–127.
11. Putnam, T. J. The use of thrombin on soluble cellulose in neurosurgery. *Ann. Surg.*, 1943, *118:* 127–129.

EXPERIMENTAL TRAUMATIC CEREBRAL CYSTS IN THE RABBIT

MURRAY A. FALCONER, M.Ch., AND DOROTHY S. RUSSELL, M.D.*
Nuffield Department of Surgery, Oxford, England

(Received for publication April 5, 1944)

IN THE COURSE OF certain experiments on the rabbit's brain we have performed a standard decompressive operation in about 270 animals (Russell and Falconer, 1941;[2] Falconer, McFarlan and Russell, 1943[1]). Apart from the main results in these experiments we have noticed, as an apparently independent side-issue, certain pathological changes in the subcortical white matter beneath the centre of the site of operation in about 50 per cent. of the animals, with the formation of a cavity or cyst in about 30 per cent. These changes appear to be intimately associated with cerebral herniation, and we now report them since they may have some bearing on the pathogenesis of traumatic cerebral cysts in man.

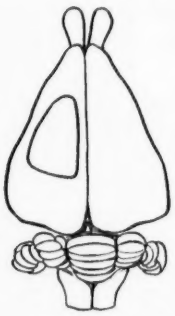


FIG. 1. Diagram of rabbit's brain indicating operation area.

The operation has been described elsewhere.[2] As shown in Fig. 1, a triangular opening, measuring from 1.5 to 2 by 1 cm., was made in the skull over the centre of the left cerebrum, the dura reflected over the margins of the bone and the incision in the scalp then closed. Asepsis was preserved and care was taken, except where certain antiseptic solutions were applied, to avoid damaging the surface of the brain. During the operation we often noticed that the brain bulged a little through the opening, and that the leptomeninges were then somewhat engorged. In animals killed within a week of the operation it was usual to find slight degrees of herniation, measuring 2 or 3 mm. in height. In some a greater hernia, up to about 6 mm. high, was formed. These larger hernias could be palpated through the scalp but, if the animal was allowed to live, they usually subsided by the end of the first week after operation. At later stages the brain was generally found at autopsy to be flush with the pericranium.

The early stages of cyst formation, observed during the first week after operation, were studied in 34 animals used for our investigations on antiseptics (1941[2]). Some of these were control experiments in which normal saline had been applied to the brain, while others had been treated with agents causing negligible damage (proflavine sulphate and sulphonamides).

The later stages (from 2 to 7 weeks) were observed in 40 animals in the course of experiments on brain abscesses (1943[1]). In this investigation the operation of decompression already described formed a preliminary stage

* Working for the Medical Research Council.

and inoculation of the brain with living organisms was not undertaken until at least 10 days later. In 7 animals a palpable hernia was detected after the preliminary operation and these were therefore set aside and killed a few weeks later without further interference. In the remaining 33 animals either the inoculation failed or the resulting abscess was remote from the cyst. In addition there were 10 animals in which scars, or scars and necroses, were unaccompanied by cyst formation; these form a closely allied group.

METHODS OF FIXATION AND STAINING

The animal was killed with chloroform and was usually perfused through the aorta with normal saline followed by 10 per cent. formaldehyde. In 8 of the animals surviving to later stages perfusion was omitted for control purposes. After further hardening in the fixative the brain was divided into coronal slices about 2 mm. thick. Selected slices were embedded in paraffin wax and sections were stained with Ehrlich's haematoxylin and eosin, Weigert's iron haematoxylin and van Gieson's mixture, Weigert's fuchselin for elastic fibres with a neutral red counterstain, phosphotungstic-acid haematoxylin and, in some instances, with Loyez' haematoxylin for myelin. Other slices were cut on the freezing microtome and sections were stained by Hortega's silver carbonate methods for microglia, neurofibrils and reticulum. Some of the microglial preparations were counterstained with Sudan III.

HISTOLOGICAL EXAMINATION

Early Changes (First week after operation).

Macroscopic. In a few of the animals the subcortical white matter beneath the centre of the decompression contained a poorly defined area of pinkish-grey softening which, in some,

FIG. 2. Early stage (5 days) showing splitting along junction of cortex and white matter, oedema and haemorrhages in white matter and engorgement of some cortical vessels. Arrows at (1) medial and (2) lateral border of decompression. Haematoxylin and eosin. ×10.

was stippled with punctiform haemorrhages. In most there was a well-defined oval, crescentic or comma-shaped cavity at the junction of the cortex and white matter which contained clear fluid or, rarely, blood clot (Fig. 2). The walls of the cyst often contained small areas of haemorrhage. The larger of the cavities measured about 4 mm. from side to side, 2 mm. in depth and from 6 to 8 mm. antero-posteriorly. Occasionally a second cavity lay deep to and parallel

with the first, occupying the white matter close to the dorsal wall of the ventricle (Figs. 3 and 4).

Microscopic. Whether a cyst was present or not the white matter in the affected area was rarefied by gross oedema and small patches of diffuse haemorrhage, often extending to the wall of the ventricle. Fragmentation of the myelin sheaths and rupture of the axis-cylinders, with the formation of retraction-balls on the severed ends, were found in the more severely damaged areas. Blood vessels, included in or adjacent to, such foci often showed fibrinoid necrosis of their walls. Leucocytes were absent or sparse. On the other hand, in animals which lived for 2 days or longer, the microglial cells were focally increased in number and had under-

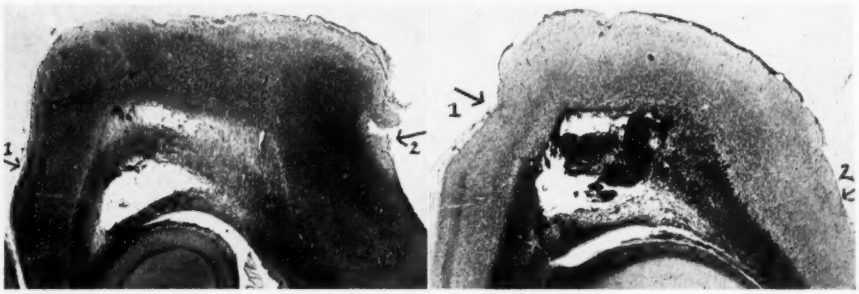


FIG. 3 (*left*). Early stage (4 days) showing gross herniation at site of operation and cysts (a) at junction of cortex and white matter and (b) between laminae of white matter. Arrows at (1) medial and (2) lateral border of decompression. Phosphotungstic-acid haematoxylin. ×8.

FIG. 4 (*right*). Early stage (2 days) showing duplication of cysts as in Fig. 3, with haemorrhage (dense black areas) and great oedema in white matter. Arrows at (1) medial and (2) lateral border of decompression. Loyez' haematoxylin. ×8.

gone amoeboid changes. The adjacent cortex showed also some activation of microglial cells and chromatolysis in a variable proportion of the pyramidal cells. The tissues surrounding the larger perforating veins were sometimes oedematous and such veins were greatly engorged (Fig. 2).

Stages in cyst-formation could be traced in the subcortical areas of oedema and haemorrhage. An early stage is shown in Fig. 2. In this animal the usual decompression had been made on the left side and 0.2 c.c. of eusol injected into the right cerebrum in order to raise the intracranial pressure and promote an appreciable hernia. The animal was killed 5 days later and a hernia 4 mm. high was disclosed. A ragged cavity occupied the junction of cortex and white matter beneath the centre of the hernia; below this the white matter was oedematous and contained many small haemorrhages. In other examples the microscope revealed a cavity with ragged walls which was too small to be seen with the naked eye. Occasionally the subcortical cyst was accompanied by a second and deeper cyst (Fig. 3). These deeper cysts arose at a well-defined plane between two layers of myelinated fibres, the more superficial fibres being oblique and the deeper parallel with the plane of the section (Fig. 4). The white matter forming a bridge between the two cysts was always severely affected by oedema and haemorrhage. It appeared probable that the cavities ultimately fused as suggested by Fig. 6, taken from a later stage, because a similar reduplication of the cysts was never demonstrated at these later stages.

The walls of the cavities, whether large or small, were composed of oedematous white matter, in parts of which haemorrhage was usually present. By the end of 8 days an appreciable number of amoeboid microglial cells had assembled in the margins of the cavity. No alterations were found in either arteries or veins in the adjacent leptomeninges.

Later Changes (Two to seven weeks).

Macroscopic. The characteristic appearances of a well-defined cyst are shown in Fig. 5. In this animal a hernia of moderate size was palpated during the first 4 to 5 days after operation. It was killed 2 months later and the brain removed without perfusion of the vessels. The cyst occupies the junction of cortex and white matter and attains its greatest diameter in the third slice in the left-hand column, which was taken from the centre of the decompression. A thin layer of white matter separates it from the lateral ventricle, which is slightly dilated. In 6 examples the cyst communicated with the ventricle (Fig. 6) but only a portion of the floor was defective, as shown in Fig. 7 which is taken from the same specimen at a more anterior level. Fig. 7 also shows interruption of the main cavity by a vertical septum: a similar loculation was seen in a few other specimens. But in many cases the cyst was merely a narrow slit or crescent; such examples are illustrated by Figs. 8 and 9.

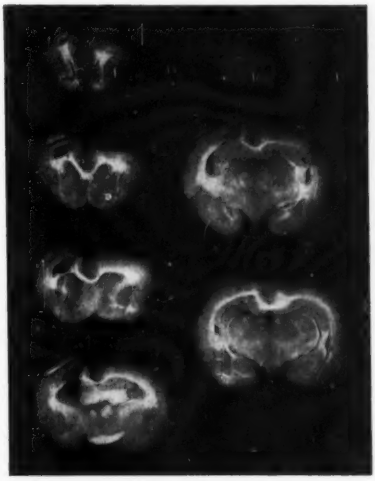


FIG. 5. Late stage (2 months). Coronal sections of brain showing traumatic cyst beneath site of decompression (see text).

Microscopic. The walls of these cysts were usually composed of a smooth, uninterrupted layer of closely felted neuroglial fibres in which the bodies of astrocytes could be seen (Fig. 10). The gliosis gradually diminished towards the adjacent nervous tissues. In addition there was a variable infiltration of the walls with foam-cells containing sudanophil lipoid. This infiltration was seldom great on the superficial or cortical aspect of the cyst, but often constituted large masses where the wall was formed by white matter. In some specimens the foam-

FIG. 6. Late stage (5 weeks). Cyst communicating with lateral ventricle. The shape of the cyst suggests that it was originally duplicated as in Figs. 3, 4. The dorsal part of the choroid plexus is dislocated into the deeper compartment of the cyst. Arrow at cortical scar in medial border of decompression. Silver carbonate. ×10.

cells formed bosses projecting into the lumen; in others trabeculae of these cells supported by glial and collagenous fibers, traversed the cavity (Fig. 7). Iron pigment was usually present in some of the foam-cells but fresh haemorrhages were rare. There was no haemogenetic cellular infiltration. Reticulum fibrils were scarce except at the dorso-medial angle of the cyst. Here it was common to find a linear vascularised scar composed of glial and collagenous fibres,

FIG. 7. Same specimen as in Fig. 6 at more anterior level to show loculation of cyst by trabecula of glia and collagen bearing a mass of foam-cells on its right wall. Arrows at (1) medial cortical scar and (2) lateral border of decompression. Haematoxylin and eosin. ×10.

FIG. 8 (*left*). Cyst (3 weeks) at junction of cortex and white matter with cortical scars over its dorsal and lateral aspects. Arrows at (1) medial and (2) lateral borders of decompression. Phosphotungstic acid haematoxylin. ×9.

FIG. 9 (*right*). Slit-like cavity (5–6 weeks) at junction of cortex and white matter. Slight diffuse gliosis in cortex at its medial angle. Phosphotungstic-acid haematoxylin. ×9.

in the meshes of which were a variable number of foam-cells containing iron pigment and lipoid. This scar extended from the wall of the cyst to the surface of the brain at the medial lip of the hernia (Figs. 6 and 7).

The 10 examples in which scars alone, or scars and necroses, were unaccompanied by cyst-formation form an allied group which seems to be attributable to the same damaging mechanism. The position and size of these lesions corresponded to the cysts already described. Fig. 11 represents a transitional form in which the cortical scar at the medial lip of the hernia almost immediately broadened into a fissure in continuity with a subcortical patch of necro-

sis. The borders of the necrotic area were unevenly infiltrated with foam-cells. Fig. 12 shows a further variation: in this the scar, which was composed mainly of collagen, expanded into a patch of foam-cells in the white matter. The patch was limited ventrally by gliosis and dorsally by an ill-defined, narrow zone of collagen fibres. A thin tongue of these fibres was continued laterally along the junction of cortex and white matter towards the external capsule. In both these animals a hernia had been palpated during the first few days after the opera-

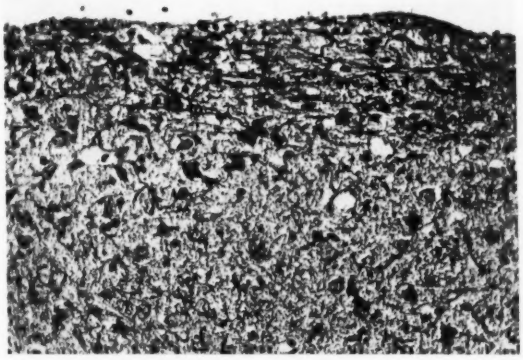


FIG. 10. Dorsal border of cyst in same specimen as in Figs. 6, 7 showing neuroglial fibres and astrocytes. Phosphotungstic-acid haematoxylin. ×240.

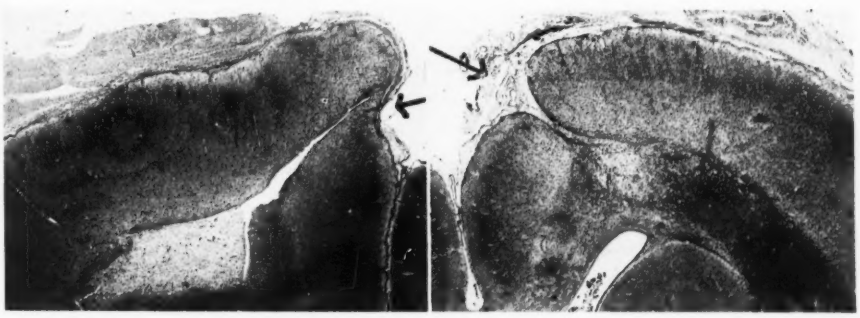


FIG. 11 (*left*). Fissured scar in medial lip of hernia (arrow) uniting with area of necrosis in subcortical white matter (see text). Haematoxylin and eosin. ×10.

FIG. 12 (*right*). Scar in medial lip of hernia (arrow) expanding into patch of foam-cells in subcortical white matter (see text). Haematoxylin and van Gieson's mixture. ×10.

tion. Both were killed after an interval of 3 weeks. In 4 other examples in this group a linear glial scar, associated with a few macrophages containing iron pigment, was identified at the junction of the cortex and white matter without further histological abnormality. In an additional example a cortical scar at the medial lip of the hernia was continued as a similar glial scar which curved ventro-laterally towards the upper border of the external capsule.

In a few examples the medial cortical scar was composed of glial fibres only. A similar scar, descending vertically into the cortex at the lateral border of the decompression, was ob-

served in a few instances: such lateral scars were never as conspicuous or as frequent as the medial scars.

While the cortex over the cyst, apart from such scars, was often well preserved when the cyst was small, there were varying degrees of atrophy and gliosis or even of complete necrosis of the whole depth of the cortex in association with some of the larger cysts. In one such example, killed 5 weeks after operation, the cortex in the decompressed area resembled an anaemic infarct; its borders were sharply defined and, except for a number of foam-cells in the superficial layers, there was no inflammatory reaction. In a second example of this kind, killed 3 weeks after operation, all but a small central area of the necrotic cortex was replaced by foam-cells: the underlying cyst communicated widely with the ventricle. No alterations in the meningeal blood-vessels were observed either in these or in any other animal of this later series.

PATHOGENESIS

The character of the histological changes observed within the first week in the white matter beneath the site of operation points to their origin in some circulatory disturbance. Their intimate association with herniation of the brain at the same site suggested that the mechanism might be a venous obstruction arising through compression of the superficial cerebral veins against the margins of the bony opening. This might in particular operate in respect of the larger veins proceeding towards the superior longitudinal sinus, especially as the hernia invariably showed its greatest development along the medial border of the opening. To test this theory we made the following experiments:

I. In 4 rabbits a small burr-hole, less than 5 mm. in diameter, was made and one of the larger cerebral veins divided through a small opening in the dura close to the superior longitudinal sinus. Haemostasis was easily secured with a muscle-stamp. The wound was then closed.

II. In 2 rabbits the usual decompression was made and the two large cerebral veins in the area were divided both near the longitudinal sinus and also near the lateral border of the decompression. The dura was left intact over the brain except at these points of division, thus preventing the occurrence of herniation. As before haemostasis was achieved with muscle-stamps.

In both groups the animals were killed at a period between 6 and 14 days after the operation, but in none was any alteration found in the white matter beneath the site of operation.

From these experiments it is clear that the collateral circulation in the rabbit's cerebrum can provide for such contingencies as the interruption of one or more of the larger superficial cerebral veins, and we are obliged to suppose either that a more widespread interference with the venous supply is necessary to produce the results that we have described, or that some alternative mechanism is responsible.

Such an alternative may be found in the physical stresses exerted upon the brain tissue in the process of herniation through an opening with rigid margins. The constancy with which the cysts and necroses occurred at the junction of the cortex and white matter, while secondary cysts arose at a deeper level along the plane separating two distinct strata of myelinated fibres, suggests that their site of origin was determined by structural factors.

In other words, when brain tissue is subjected to a physical strain of this nature the positions in which cleavage will occur will be determined in some measure by differences of consistency such as the transition from grey to white matter, or the alignment of tracts of myelinated fibres within the white matter. In this connection it may be noted that the facility with which such tracts may be separated from one another in the hardened brain has formed the basis of several established methods of blunt anatomical dissection.

But physical forces alone will not cause changes such as we have described: pathological processes play an essential part. This was clearly demonstrated by our inability to produce any comparable splitting of the brain in a series of 4 freshly killed rabbits. In these we made the usual opening in the skull and injected a stiff solution of gelatin into the meningeal spaces at the base of the cerebrum by passing a needle forwards through the cisterna magna. Enough of the gelatin was injected to produce a hernia of a size similar to those seen in our experimental animals. The brain was removed from the skull after being fixed and hardened *in situ*. On section no abnormality was found in the tissues at the site of herniation. It therefore follows that, within the limitations of our experiments, splitting of the tissues will not occur unless they have undergone certain pathological changes with resultant softening. Such changes may be induced directly through the action of physical forces (see following paper by Holbourn) or indirectly through the distortion of blood-vessels brought about by herniation.

We are not competent to discuss the physical forces involved but are greatly indebted to Dr. A. H. S. Holbourn for his help and criticism in this field. In the following paper he has briefly explained the principles involved and their application to the particular problem of these traumatic cysts.

We wish to thank Professor J. A. Gunn for help in the maintenance of our animals and Professor Hugh Cairns for his advice and interest. We gratefully acknowledge a special grant for expenses from the Medical Research Council.

REFERENCES

1. Falconer, M. A., McFarlan, A. M., and Russell, D. S. Experimental brain abscesses in the rabbit. *Brit. J. Surg.*, 1943, *30:* 245–260.
2. Russell, D. S., and Falconer, M. A. Antiseptics in brain wounds. An experimental study of the histological reaction of cerebral tissues to various antiseptic solutions. *Brit. J. Surg.*, 1941, *28:* 472–499.

THE MECHANICS OF TRAUMA WITH SPECIAL REFERENCE TO HERNIATION OF CEREBRAL TISSUE

A. H. S. HOLBOURN, M.A., D.PHIL.
Nuffield Department of Surgery, Oxford, England

(Received for publication April 5, 1944)

THE GENERAL theory of trauma will be developed in this paper by means of the theory of elasticity. Once the theories of trauma and intracranial mechanics have been put on a firm basis, it is possible to discuss particular examples of traumatic intracranial tissue damage, and to compare the theoretical predictions with the observed facts, thereby testing the general theory. The experimental investigation of herniation of cerebral tissue through a defect in the skull, reported in the preceding paper by Falconer and Russell, is an excellent subject on which to test the general theory. Because of the definite nature of the experiments, and the results obtained, the test of general theory is stringent. It will be shown that there is good agreement between theory and experiment.

THE FUNDAMENTAL CONCEPTS OF THE THEORY OF ELASTICITY

The theory of trauma is really a branch of the theory of elasticity. Hence, before the theory can be developed, it is necessary to have a general understanding of the theory of elasticity. A simple explanation of the underlying principles is given to help readers who may be unfamiliar with the subject.

The technical meaning of the word stress is a force per unit area. It is quite different from strain, which is roughly speaking a displacement of one part of a body relative to another part. A strain may often be regarded as the consequence of a stress.

A hydrostatic pressure is an example of a simple type of stress. It is uniform in all directions. The pressure of cerebrospinal fluid in the ventricles is a true hydrostatic pressure. But elsewhere in the brain, at any rate in many pathological conditions, the stress system is vastly more complicated, so that it cannot be described by one single quantity such as hydrostatic pressure. A complete specification of the state of stress at any point within the brain substance requires six components at each point. Only when three of these components are all equal, and the remaining three are all zero is there a hydrostatic pressure at the point considered. This will not in general be true. Hence the expression "intracranial pressure" is in general meaningless and will be avoided in what follows. It is well known (Cairns, 1939[1]) that one single quantity, such as "intracranial pressure," having the same value throughout the brain does not adequately describe conditions in the brain where expanding tumours are present. It often appears somewhat as if the hydrostatic pressure were higher near the tumour than elsewhere. It

is not sufficiently realised, however, that different hydrostatic pressures could not coexist at two points in the brain unless there also existed non-hydrostatic stresses at other points.

It is convenient to divide the six components of stress into two sets of three which are of different types. Three consist of forces acting perpendicular to surfaces and are called pressures or tensions, and three consist of forces acting tangential to surfaces and are called shearing stresses. From the point of view of their destructive effect on substances, the shearing stresses are much more important than the others.

These shearing stresses are responsible for a sliding motion of one layer of a substance upon another. As a representation of what happens one may consider a neat and squarely piled pack of playing cards. If, by applying the palm of the hand to the top card and pushing in the direction of the surface of the card, one could slide each card a little relative to the one below, so that the pack changed from the shape shown on the left hand side of Fig. 1 to that shown on the right, then it would be a representation of a shearing

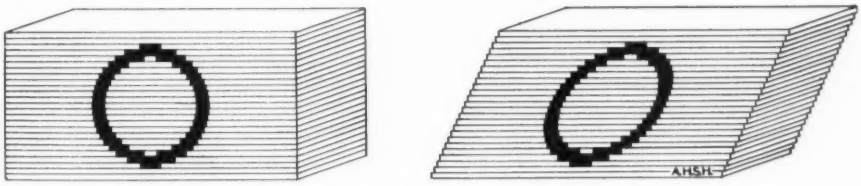


FIG. 1. Pure shear strain in a pack of cards. Note that the circle is deformed into an ellipse—an example of a shear ellipse.

stress causing a shearing or sliding strain. Note that the shape on the side of the pack has changed from a circle to an ellipse. This is an example of a strain ellipse.

It is often helpful to have a mental picture of the stresses at a point in a body. A hydrostatic pressure, which is a stress uniform in all directions, may be visualised as a sphere, which is obviously a shape that is uniform in all directions. The diameter of the sphere represents the magnitude of the pressure. The most general stress system at a point may often be visualised as a shape like a plum stone or ellipsoid, having an existence at the point considered. The pressure is greatest in the direction of the longest axis of the ellipsoid, and least in the direction of the shortest axis, and so on. A body subjected to the most general type of stress may be thought of as filled with little ellipsoids whose sizes, proportions and orientations vary from point to point in the body.

If the pressure is a purely hydrostatic one, represented by a sphere, there are no shearing stresses. But if the pressure is not a hydrostatic one—i.e., if its representative sphere has been distorted into an ellipsoid—shearing stresses are present. The greater the difference between the largest and

smallest diameters of the ellipsoid, the greater the amount of shearing stress present. This difference may be used as a measure of the shearing stress at the point considered. The shearing stress is thus seen to be a measure of the degree to which the stress system departs from a purely hydrostatic pressure. It follows that even when a rod, or wire, is under pure tension, shearing stresses are present.

An ellipsoidal type of stress may be regarded as the cause of an ellipsoidal type of strain. An ellipsoidal strain is easily visualised. If the material at a point in a body undergoes an ellipsoidal type of strain, then a small sphere surrounding the point considered becomes distorted into an ellipsoid. This phenomenon was exemplified in two dimensions when the circle on the pack of cards became distorted into an ellipse. A good representation of shearing strains comes from pathology. The renal glomeruli in the neighbourhood of an expanding lesion which are originally spheres become distorted into ellipsoids whose orientation and proportions vary from point to point. Hence a kidney in which the glomeruli are thus distorted has certainly been subjected to an ellipsoidal type of stress system, and shearing stresses were certainly present.

THE APPLICATION OF THE THEORY OF ELASTICITY TO ELASTIC FAILURE AND CRACK FORMATION IN INANIMATE MATTER

Before a substance breaks it exhibits the phenomenon of elastic failure. If a substance is stressed sufficiently to exhibit the phenonemon, it will not return to its original condition when the stresses are removed. The substance has, in fact, been permanently damaged. As the practical man would put it, it has acquired a permanent bend, stretch, or other distortion. The usual criterion for elastic failure is that the shearing stress must exceed a certain critical value. In other words, the stress system must differ from a hydrostatic pressure by a certain critical amount. Once elastic failure has occurred at any spot, the material is liable to start to crack there, particularly if the stresses fluctuate in intensity. In most substances the crack is in that plane which has the greatest tension* across it—i.e., at right angles to the longest axis of the stress ellipsoid. A crack starts at the point of the substance where the shearing stress is a maximum, but as it runs in a direction determined by the tension it may soon get out of the region of high shearing stress. It will then stop.

But if the substance has a grain, like wood, the phenomenon of cracking is somewhat altered. A crack starts, as before, where elastic failure has occurred; and, as before, elastic failure is most likely to occur at the points where the shearing stress is a maximum. Once started, a crack tends to run in the direction of the grain. To take a familiar example: when an unskilful person drives a nail into a piece of wood the wood always starts to split at

* The material can crack even if there are only pressures acting upon it and no tensions. In this case it still cracks in the direction given by the above rule if one mathematically superposes on to the existing stress system a large negative hydrostatic pressure.

the nail, where the shearing stresses are highest, and always runs in the direction of the grain. If, in the case of a piece of wood, there is a tension at right angles to the direction of the crack, then the two sides of the crack are pulled apart and an actual gap is formed. But wood can also crack in the direction of the grain, owing to a sort of shearing collapse. When this happens the layer on one side of the crack is forced to slide along the layer on the other side in just the same way as one card in Fig. 1 is forced to slide along the card beneath it. In this case no actual gap appears.

THE APPLICATION OF THE THEORY OF ELASTICITY TO TISSUE DAMAGE AND CYST FORMATION

The brain, like inanimate substances, can be permanently damaged by being subjected to too great a stress. It is *a priori* not unreasonable to suppose that the criterion of permanent damage or injury to cerebral tissue is that the shearing stresses must exceed a certain critical value, just as with inanimate substances. Hence the liability to injury is proportional to the amount by which the stress departs from a purely hydrostatic pressure.

If the stresses only slightly exceed the critical value, probably no catastrophic phenomenon analogous to the formation of a crack in inanimate matter will occur. The comparatively mild injury which results can therefore be repaired by scar formation. Hence if scarring occurs under these conditions there will be a permanent record of the regions which were initially subjected to high shearing stresses.

But if the shearing stresses in any region are much above the critical value it is probable that phenomena analogous to cracking arise. The high shearing stresses injure the brain substance, so that it becomes unable to withstand them, and tears. The tear will start in the region of highest stress, but it may soon move out of this region, as its direction will be largely determined by the predominant fibre direction. If it tears under the action of tension perpendicular to the fibre direction, the fibres will be pulled apart and a cyst will develop. But the tear may also be a sort of shearing collapse, and the fibres will have no tendency to be pulled apart, but only to slide relative to one another. In this case there will be no tendency to cyst formation. Instead the injury will be easily repaired by gliosis, and a cross section of the region will exhibit a linear glial scar.

Of course, if the stress enormously exceeds the critical value, physiological or pathological considerations do not enter into the question. The brain will behave exactly like inanimate substances, as happens, for example, under the surgeon's knife.

THE CORRESPONDENCE BETWEEN THE BEHAVIOUR OF INANIMATE MATTER AND BRAIN TISSUE

On the above theory there is an exact parallel between the behaviour of cerebral tissue and the behaviour of inanimate substances, brain damage corresponding to elastic failure and cyst formation to fracture. The existence

of some such corresponding principle may be inferred from a comparison of Figs. 6, 7, 12 (Falconer and Russell) with Fig. 2, and Figs. 5 etc. (Falconer and Russell) with Fig. 3. Fig. 2 shows the effect of applying pressure to a

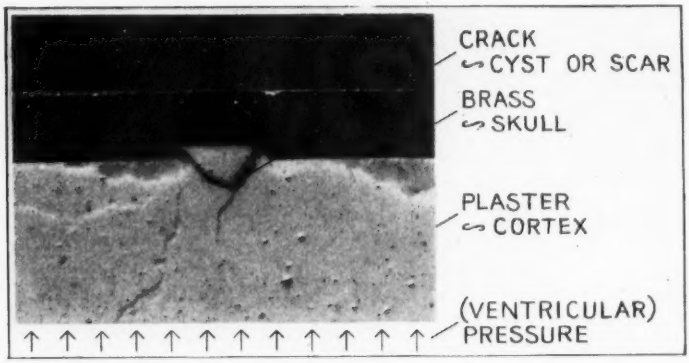


FIG. 2. Plaster of Paris brick, broken by being forced up through an opening. The crack starting at the edges of the opening corresponds to the glial scars shown in Figs. 6, 7, 12 etc. of the preceding paper.

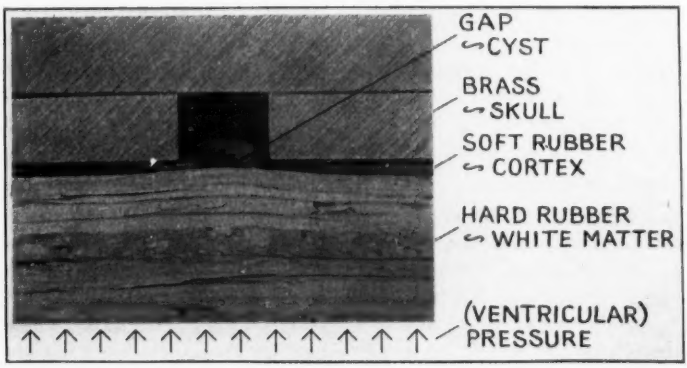


FIG. 3. Pressure forcing a layer of soft rubber backed by a layer of hard striated rubber through an opening. The soft rubber tends to get squeezed farther through the opening than the hard rubber, so that a gap forms between the two. Compare this gap with the cyst shown in Figs. 5 etc. of the preceding paper.

plaster of Paris brick that has one face in contact with a piece of brass in which there is an opening. The plaster of Paris corresponds to cortex, and the brass to skull. The scarring at the edges of the decompressions in Figs. 6, 7, and 12 (F. and R.) has a partial correspondence with cracks at the edges of the opening in Fig. 2. The correspondence is rigorous at the very edges of the opening, but elsewhere it is somewhat fortuitous, in spite of being strik-

ing. Fig. 3 shows the effect of applying pressure to soft rubber backed by a layer of harder rubber. The soft rubber represents cortex, which is slightly less rigid than white matter. The pressure causes a gap with a crescent-shaped section to form at the junction between hard and soft rubber. This gap corresponds rigorously to the cysts shown in Figs. 5 etc. (F. and R.). The agreement between theory and actuality is in this case very striking.

THE DETAILED APPLICATION OF THE THEORY TO HERNIATION

It is now possible to consider in greater detail what happens when, owing to the pressure in the ventricles, the brain is herniating through an opening in the skull. As the pressure in the ventricles is a fluctuating one, due to breathing and blood pulse, the shearing stresses to which it gives rise* near the opening are also fluctuating, and therefore peculiarly liable to cause

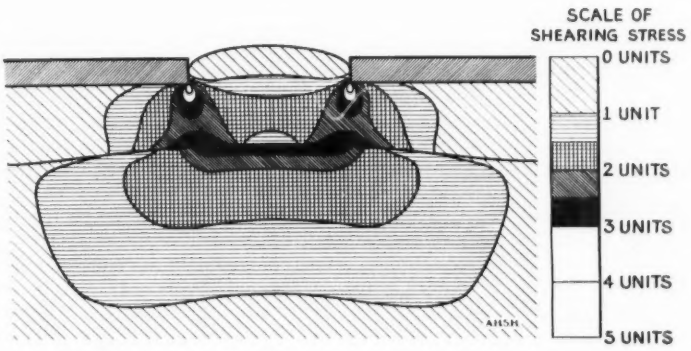


FIG. 4

FIG. 4. Shearing stresses which arise in a layer of more rigid material backing a layer of less rigid material, when they are forced up through an opening. Compare the areas of greatest shearing stress in this figure with the areas of greatest damage in the figures of the preceding paper.

damage to the brain substance. Fig. 4 shows the shearing stress system in the case of a more rigid substance backing a less rigid one, corresponding to white matter and cortex respectively. The thickness of the layer corresponding to cortex is half the breadth of the opening. In accordance with what has been said before, the figure gives the amount by which one would be in error if one assumed that the "intracranial pressure" was a purely hydrostatic pressure. The figure shows at each point the difference between the longest and shortest axis of the stress ellipsoid at that point. But it gives no indication of the directions of the axes of the stress ellipsoids.

* It might be thought that it is wrong to say that the ventricular pressure causes the stresses in the brain substance because stresses in the brain substance, such as arterial tension, obviously cause pressure in the ventricles. Actually, each contention is equally true or false. The ventricular pressure is in equilibrium with the complicated stress system in the rest of the brain and *vice versa*. But, since the ventricular pressure is easily visualised and easily measured, it forms a convenient logical starting-point when considering the intracranial stress system.

The stresses shown in Fig. 4 can be obtained in a number of different ways. The actual method adopted was a photoelastic one. Circularly polarised light was passed through a gelatin model of the cross section in which one was interested and analysed in a circular analyser. A grid was placed in front of the gelatine and the isochromatics plotted.

The photoelastic model was made as follows. Six per cent. gelatine, corresponding to white matter, was made first and allowed to set. Then a 1.25 cm. thick layer of 3 per cent. gelatine at a temperature of 45°C. was poured on top and allowed to set. As the junction between the two layers showed signs of stress, the whole was annealed by allowing to stand for some days in a warm room. When thoroughly annealed the jelly was melted on the outside by dipping the container in hot water, and slid to the other end of the container in which was the opening through which the jelly sagged, both through its own weight and the weight of some water on top of it. The breadth of the opening through which the jelly herniated was 2.5 cm.—i.e., twice the thickness of the superficial layer of gelatine. The thickness of the gelatine in the line of vision was 5 cm. Colours appeared up to the 5th order.

It should be noted that the model is not exact, for a number of reasons. It is effectively two-dimensional, whereas the brain is three-dimensional. It would be a correct model only if one coronal slice of brain exerted no shearing forces on its neighbours on either side. This is not the case; but near the central section of the decompression no very large errors are introduced on this account. Further, the units of stress used in the figure are probably different for the 6 per cent. gelatine and the 3 per cent. But this is unimportant, as it is improbable that equal stresses in white matter and cortex cause equal damage. Another deficiency in the model is that the brain is not a homogeneous material like a jelly, but has a grain. This does not have much effect on the initial stress distribution, before tearing or cyst formation. But once a tear or cyst has started, it will tend to run in the direction of the fibres; and this will in general be different from the direction it would have taken in a grainless substance.

There is no particular virtue, other than convenience, in using gelatine. The fact that it and the brain have somewhat the same consistency is a coincidence. Glass or steel would give just the same stress pattern.

Fig. 4 shows that in the section considered there are two main regions of high shearing stress. (1) A large mountain of shearing stress in the white matter over the centre of the defect in the skull. This covers a large area, and has a pronounced ridge just inside the junction between white matter and cortex. (2) Two walls of shearing stress running straight across from the edges of the defect to the white matter. These walls have high pinnacles at the edge of the defect, and lesser summits where they join the white matter.

(1) From the existence of the large mountain of shearing stress in the stiffer substance, one can predict a large injured area in the white matter, increasing in severity of injury the closer it approaches the junction with the cortex. The large area of haemorrhagic softening, which is shown at an early stage in Fig. 2 (F. and R.), and which has its maximum at the junction between white matter and cortex, is therefore in agreement with theory.

The theoretical distribution of shearing stresses has a very high ridge in the stiffer substance just at the junction between the layers of different consistency. This may correspond to the observation on page 187 (F. and R.) that "In 4 other examples in this group a linear glial scar . . . was identified at the junction of the cortex and white matter".

On the other hand these glial scars may mark the position of previous small cysts. As that portion of the junction between cortex and white matter which lies directly over the centre of the opening is the most injured, it will be the most likely part to be torn by the stresses. The stress here is a tension perpendicular to the surface of junction. That the tension is in this direction is borne out by the appearance of the gap in Fig. 3. It is clear that any small connexion running across this gap would tend to be torn as the gap was formed. Therefore, the stress must be equivalent to a tension tending to pull the walls of the gap apart. At the ends of the gap this tension changes over gradually to a pressure tending to press the surfaces together. This is what determines that the gap shall be just the length that it is. Since, therefore, there is a tension across the surface of junction between cortex and white matter, the injured surfaces at the junction will tend to be pulled apart, and a cyst will tend to form.

The linear glial scars at the junction between cortex and white matter may possibly therefore mark the position of small cysts. That such cysts tend to form can be seen from Figs. 5, 9, etc. (F. and R.), which show cysts in the predicted position and of about the predicted length.

The inner cyst shown in Figs. 3 and 4 (F. and R.), is another example of the high stresses set up at a boundary between layers of different consistency —the difference in consistency being caused in this case by a difference in fibre direction. It is, perhaps, pertinent to remark that the writer was able to say that there should be some such difference before he saw the slide reproduced in Fig. 4 (F. and R.).

It is important to notice that a shearing stress diagram, such as Fig. 4, gives only the position of injuries; further information, not given by the diagram, is necessary before one can decide whether such injury can be easily repaired by gliosis, or whether it will lead to the formation of a cyst. An easily visualised example of this is given by the following hypothetical case. (It bears some resemblance to the more practical case of an indriven portion of bone.) Suppose a brain which is everywhere adherent to the inner surface of the skull. Suppose that an opening similar to the one considered is made in the skull. Suppose finally that the atmospheric pressure is considerably greater than the ventricular pressure, so that the brain bulges in at the opening instead of out. In this case, the picture of the shearing stress distribution would, by a curious coincidence, be exactly the same as in Fig. 4. But all the pressures would be replaced by tensions and *vice versa*. Hence, in these circumstances, we should have, on our hypothesis, tissue damage in exactly the same place as we have now, but no cyst at the junction of cortex and white matter. Instead of the top and bottom walls of the cyst being pulled apart by the tensions, they would be kept in apposition by the pressures; and no cyst would form in the position already described.

(2) Running in from the edges of the opening in the skull, are two walls of high shearing stress in the less rigid substance. Damage is therefore to be expected in this region. Figs. 7, 11, and 12 (F. and R.) show cortical scars

which may simply mark the position of these walls of stress. On the other hand, the scars are somewhat more linear than one would expect—this suggests that there may have been a certain amount of shearing collapse, starting from the very high pinnacles of stress at the edges of the opening, and running in the predominant fibre direction. Provided no large cyst or softened region formed at the junction between cortex and white matter deep to the centre of the opening, there is very little tendency for a cyst to form in the region of these scars, because there is little stress in the nature of a tension tending to pull apart the injured tissues. The main stress in this region consists of a shear stress acting tangentially to the fibre direction. This prevents the brain from being pushed out through the opening. Hence the main tendency will be for the brain above the opening to slip relative to the rest of the brain, and there will be little tendency for a gap, or cyst, to form. Figs. 6, 7, 9 and 12 (F. and R.) show that there is little tendency to form cysts in this part of the cortex.

Of course, whether or not any shearing collapse has taken place, the scar is more likely to be seen in the superficial parts of the cortex, because, as shown in Fig. 4, the stresses are greatest there. This is borne out by Figs. 6, 7 and 12 (F. and R.).

The main reason why the medial scar is more marked than the lateral, is that the medial border is near the great longitudinal fissure. The brain is thus more liable to slip out at the medial border of the decompression because there is only a small strip of skull holding it in. Hence the strains are greater there, and consequently the stresses.

There are minor summits at the deeper ends of the walls of shearing stress. These might possibly act as starting points for lines of shearing collapse running across to the edges of the opening. But, once the main cyst has formed at the junction between cortex and white matter, these minor summits become larger, and in addition, a tension develops across the fibre direction, tending to separate the fibres. (Clearly the loosened cortical layer stretching from side to side of the opening is being bent outwards at this point, and must, on its inner surface, be in a state of tension perpendicular to the fibres.) Hence conditions now favour the formation of a cyst in the cortex, starting from the region where it joins the white matter. Fig. 11 (F. and R.), shows such a cyst.

The anaemic infarct which sometimes occurred in the cortex under the decompressed area (p. 188, F. and R.) occurs in a comparatively unstressed region. The writer would therefore guess that it is a secondary phenomenon due to its being, in the early stages of the process, separated from the rest of the brain by a complete envelope of damaged tissue. If the damage were sufficiently severe, anoxaemia would result.

THE EFFECT OF PLASTIC CREEP

The stress system shown in Fig. 4 is the initial stress system immediately after the decompression is made. If brain substance were perfectly elastic,

these stresses would persist unaltered indefinitely. But brain substance is not perfectly elastic. It is, to a certain extent, plastic. That is to say, for example, if a portion of it is in tension, that portion will, if the tension persists, grow longer and longer in the course of time; when the tension is released, the portion will not return to its original length. It will have suffered a permanent change. The fact is that brain substance has no hard and fast elastic limit, because any small stress causes some irreversible alteration, though only a negligible amount in a small period of time. One can say roughly, however, that the effect of applying a stress to brain substance is an immediate elastic strain, and then a slow plastic creep. The effect of this plastic creep is most marked where the stress is high. The material yields in the highly stressed regions. This has the effect of lowering the stress there. Hence the effect of plastic creep is to wear away the tops of the mountains of stress, and fill in the bottoms of the valleys, so that the stress system becomes much more uniform. Since, in this process, the dangerous pinnacles of sheering stress disappear, the material is less likely to start to crack. The material has actually become stronger. This phenomenon is exemplified very well by a piece of pitch. If it is tapped quite lightly it will break, yet it will withstand considerable force if it is applied so gradually that the pitch has time to creep. The brain itself provides a good example of this phenomenon. The stresses in the neighbourhood of a tumour which has grown slowly to a certain size are less than those in the neighbourhood of a tumour which has grown quickly to the same size. This is probably one of the reasons why slowly growing tumours cause less disturbance than rapidly growing ones. As the diminution of the stresses with time is brought about by the movement of the substance under the action of these stresses, it is clear that a decrease of stress in the most stressed regions is accompanied by an increase of strain.

Since, therefore, the high concentrations of stress in a herniating brain are disappearing all the time, cyst formation must occur either fairly soon, or not at all.

THE EFFECT OF SIZE

The stress systems for a small animal with an opening in its skull are of exactly the same form as the stress systems for a large animal of the same shape with a proportionate sized opening in its skull. The intensities of the stresses are equal at corresponding points in the two animals. Hence one would expect the tissue damage, scars and cysts to be the same in both, except for the change in the scale of the phenomenon. (This neglects the effect of the convolutions of the brain, which tend to be more marked in animals with large brains.)

Similarly, provided the opening is not so large that it appreciably reduces the intraventricular pressure, the stress systems are geometrically similar and of the same intensity whatever the size of the opening. Hence the larger the opening the greater the size of the damaged region; but the intensity of

damage at corresponding points is always the same. (This neglects both the effect of convolutions and the effect of the varying ratio of cortex thickness to opening diameter. It also neglects the fact that a large region, damaged to a given extent, is less likely to heal than a small region damaged to the same extent.)

SUMMARY

The theory of damage to cerebral tissue is developed on the following assumptions: (1) that the brain behaves as an approximately elastic body; (2) that cerebral tissue is injured when the shearing stresses exceed a certain critical value; (3) that if the stresses present are such as to tear the injured tissues apart, then a gap, or cyst, is formed; (4) that if the stresses are such that they do not tend to tear the injured tissues apart, then no cyst forms, and the injury can be repaired directly by gliosis.

This theory is applied to the case of a brain forced to herniate through an opening in the skull, owing to the action of the ventricular pressure. The predicted positions and shapes of the injured regions of the brain are found to agree with the results reported in the preceding paper by M. A. Falconer and D. S. Russell. The predictions as to whether or not the injury will lead to cyst formation are also found to agree with these workers' results.

I should like to thank Prof. Cairns, Dr. Russell and Mr. Falconer for their help. If this paper is comprehensible to the non-physicist reader, the credit is largely due to Dr. Russell. By the kindness of Prof. Liddell, the experimental work in connexion with this paper was done in the Oxford University Laboratory of Physiology.

REFERENCE

1. Cairns, H. Raised intracranial pressure: hydrocephalic and vascular factors. *Brit. J. Surg.*, 1939, *27*: 275–294.

A REVIEW OF THE FLOREY AND CAIRNS REPORT ON THE USE OF PENICILLIN IN WAR WOUNDS

DURING THE Sicilian campaign the British Government sent Brigadier Cairns, Consulting Neuro-surgeon to the R.A.M.C., and Professor Howard Florey to North Africa and Sicily as heads of a mission to study the uses to which penicillin might be put in the treatment of war injuries. A detailed report* was promptly issued by the War Office and was made available for restricted distribution in December of 1943. Since the report was issued as a classified document it was at first impossible to give it detailed notice. Reviews, however, have now appeared both in the *British Medical Journal* (11 Dec., 1943) and the *Lancet* (11 Dec., 1943), and the War Office, through the courtesy of Major-General L. T. Poole, Director of Pathology of the R.A.M.C., has given the *Journal of Neurosurgery* authorization to give the report detailed notice.

Readers of the *Journal* will be especially interested in the sections of the report dealing with head injuries, and the editors have pleasure in being able to make these available with certain minor omissions. The material which follows appears as Section 32 (pp. 97–105) under the title "A preliminary report on the treatment of head wounds with penicillin," and is signed by Brigadier H. Cairns, the late Major K. C. Eden, R.A.M.C. of No. 4 M.N-S.U. and Major J. Shoreston, R.A.M.C. of No. 5 M.N-S.U.

* * *

For the Sicilian campaign No. 4 Mobile Neurosurgical Unit was attached to 48th General Hospital at Tripoli and No. 5 Mobile Neurosurgical Unit to 71st General Hospital at Sousse. In these two units 50 gunshot wounds and 23 head wounds due to blunt injury were treated (Table I). Cases were fewer than had been expected and arrived for treatment much later than in previous campaigns. Consequently the original plan of treating alternate cases only with penicillin was abandoned, and all penetrating brain wounds 72 hours old or older were treated with penicillin. Non-penetrating wounds—that is, wounds of the scalp and skull with dura intact—up to 16 days old were treated with penicillin; and a smaller, and in the event less severe, group were treated with sulphonamides. Non-penetrating blunt injuries, mostly from road accidents in the neighbourhood, were treated, some with penicillin and some with sulphonamides.

Bacteriological examinations were done by Major Scott Thomson at Tripoli and by Captain Ross at Sousse. In approximately one-half of the gunshot wounds a previous operation had been carried out in Sicily, sometimes with wide excision of skin and "decompression," procedures which

* Florey, H. W., and Cairns, Hugh (Brigadier, R.A.M.C.). Investigation of war wounds. Penicillin. A preliminary report to the War Office and the Medical Research Council on investigations concerning the use of penicillin in war wounds. [London] War Office (A.M.D. 7). October, 1943. 114 pp. [Not yet available for general distribution.]

made subsequent wound closure difficult. Further operation in these cases showed that in the penetrating injuries surgical cleaning of brain wounds at the original operation had invariably been incomplete.

The majority, if not all, of the patients with gunshot wounds had had sulphonamides in the forward area, both locally and by mouth. Our records of this are not complete, but it is clear that extensive courses of intravenous sulphadiazine had been given in some cases. The Eighth Army has probably become as efficient as any medical service in the forward area can be in giving sulphonamides.

Bacteriological Findings. Of 36 cases of gunshot wounds, 1½ to 16 days

TABLE I*

	No.	Fr. of skull
GUNSHOT WOUNDS		
Penetrating brain injuries (72 hours or older)	23	23
Non-penetrating (dura intact):		
Treated with penicillin	17	11
Treated with sulphonamides alone	10	3
HEAD WOUNDS DUE TO BLUNT INJURY		
Treated with penicillin	16	—
Treated with sulphonamides alone	7	2
TOTAL	73	39

* The following cases of head injury are not included in the report: 2 cases of penetrating brain injury which arrived in a moribund state and died without operation; a severe orbito-frontal wound 2 days old which gave an excellent result with penicillin and subsequent skin graft; an early case of penetrating occipital wound who burst his wound open soon after operation, but subsequently did well; a close range through-and-through bullet wound of the left hemisphere, operated on when 5 hours old and treated with penicillin, death occurring 5 days later from extensive intracranial haemorrhage and bronchopneumonia (Algiers case).

old, which were examined bacteriologically only one was sterile. *Staphylococcus aureus* was found in 23 cases and pneumococcus in one. Haemolytic streptococcus was found in four, always in association with *Staphylococcus aureus*. In the penetrating brain wounds 19 of the 22 examined were infected with gram-positive pyogens; 13 of these wounds were purulent to the naked eye. At operation in 10 cases pus was found in the superficial layers, in the scalp and temporal muscle, but was not present in the brain; in three cases both the more superficial layers and the brain contained pus. This was borne out by Major Scott Thomson's examination of material from different levels of the wound: in 11 cases so examined pyogenic organisms were found, in three cases at all levels of the wound, in six cases in the scalp only, and in two cases in the brain only.

In two cases of gunshot wound a *Staphylococcus aureus* was found to be penicillin-resistant.

In scalp wounds due to road accidents, of which two-thirds were no more and often less than one day old, gram-positive pyogens were found in only one of 11 cases bacteriologically examined.

Methods of Treatment. It will be convenient at this stage to summarise briefly the method of operative treatment for brain injuries hitherto employed in neurosurgical units of M.E.F. and B.N.A.F. The scalp edge and damaged bone are excised. The brain wound is, so far as possible, cleared of dead brain tissue, clot, hairs, missiles and bone spicules, particular attention being paid to bone spicules. The scalp is closed in two layers, and to avoid undue tension extensive plastic procedures are sometimes required. Before closure the wound is powdered with sulphathiazole, and after operation a course of sulphadiazine is given intravenously.

In the present series the wounds were excised, cleaned and sutured as before. A fine tube was passed through a stab hole into the brain cavity, or to the mouth of that cavity, and after operation for three to six days calcium penicillin solution (250 units per c.c.) was instilled at eight or later 12-hourly intervals. An additional tube for penicillin was sometimes passed into the subgaleal plane, particularly when there was "dead space," as after excision of wounded temporal muscle. The total dosage varied between 2,250 and 40,000 units per case (average 15,000 units). As experience increased the dosage was considerably reduced. In one of three cases tested, a wound of the temporal lobe not involving the ventricle (Case 20), a trace of penicillin was found in the lumbar cerebrospinal fluid 12 hours after injection of penicillin into the wound.

In addition, penicillin-sulphanilamide (1,000 or 2,000 units per gm.) was applied to the wound during dressings and occasionally during operations; the amounts expended were small, and wastage was best avoided by the use of the R.A.F. sulphonamide blower.

Intramuscular penicillin was also given to three patients who had compound fractures of limbs in addition to brain injuries. Of the non-penetrating head injuries 27 were closed after a single application of 1 to 3 gm. penicillin-sulphanilamide powder, and six were given penicillin solution through tubes. When tubes were used aspiration was performed before each penicillin injection, and as much as 25 c.c. of thin salmon-pink pus were obtained.

RESULTS

Penetrating Brain Wounds. The bacteriological results usually showed that after two days' treatment of the brain cavity with penicillin gram-positive cocci were no longer found in the fluid sucked or discharged from the wound; organisms of the coliform group were almost invariably present. In wounds which remained completely closed this state of affairs persisted until healing was complete. Where the wound gaped at any point forming a raw surface or sinus, gram-positive cocci could sometimes be grown from the surface in the later stages. In two of the cases in which *Staphylococcus aureus* reappeared in the discharge the wound bed was not completely closed,

being connected in one case with the naso-pharynx and in the other with the external auditory meatus.

There were 3 deaths among the 23 cases.

Case 17. This was a dehydrated, semi-comatose man with a thready pulse and cold extremities, who had been struck by a shell eight days before. He had a purulent wound 10 by 5 cm. in the left fronto-parietal region. In its anterior part it was surmounted by a brown brain fungus (3 cm. diam.) and elsewhere in its base bare white bone was visible. At operation three separate pneumococcal brain abscesses were emptied and 14 fairly large bone fragments were removed from near the medial surface of the left frontal lobe. There had been so much tissue loss that the wound could not be closed completely. The patient died within 48 hours of operation from spreading encephalitis. He had received up to that time only 15,000 units of penicillin, an inadequate amount for such an intense and loculated infection, and at necropsy pneumococcus and *Proteus* were still present in the wound cavity.

Case 13. A man with complete right hemiplegia and aphasia, who had received a small penetrating left temporal wound six days before. Bone chips and a large amount of blood clot were removed from his brain wound and penicillin solution was instilled for four days. He died on the seventh day after operation from a large blood clot in the left cerebral hemisphere. At necropsy there was no evidence of infection.

Case 18. This patient had multiple wounds, including a compound fracture of the left femur, and a wound of the abdominal wall for which laparatomy had been done in the forward area, with negative findings. He had also two wounds in the forehead which had been converted into one, excised and sutured in the forward area. At the base on the eighth day the head wound was seen to be healing, but X-rays showed bone fragments in the subjacent brain. At operation pus (*Staphylococcus aureus*) and necrotic material were found beneath the healing scalp and the bone chips were removed.

He was treated by local and intravenous or intramuscular penicillin for five days (5,000 units locally, 485,000 units parenterally). He became increasingly drowsy, and on the 10th day after operation his frontal wound was aspirated and 5 c.c. of pus were obtained from beneath the skin. Films of this showed no organisms and culture yielded only "B. coli." He died on the following night.

At necropsy, beneath the intact frontal wound was a button of firm granulation tissue 2.5 by 2.5 by 0.3 cm. Beneath that in the right frontal lobe was a large thin-walled abscess 5 cm. in diameter and extending backwards above the right frontal horn for a distance of 12 cm. It was filled with pink pus. The ventricular wall was intact.

Section of the abscess wall showed numerous gram-negative organisms and in one place, where there had been a tiny spicule of retained bone, clumps and chains of gram-positive cocci. The cellular components of the abscess wall showed nothing remarkable.

Comment. In the first of these three fatal cases penicillin was applied too late to control the effects of the pneumococcal infection. In the second case infection was never severe, and death was due to intracranial haemorrhage. The third patient died as a result of an error of surgical technique. If adequate drainage had been provided for the gram-negative pus he would almost certainly have survived, for his other wounds, including the compound fracture of the femur, were doing well. It is to be noted, however, that gram-positive organisms were still present at one part of the abscess wall, in which a small bone spicule was embedded.

Apart from this case the results to date as regards life may be considered as being unusually good for such old and severely infected brain wounds.

However, no case has so far been followed for more than two months, and a further period of observation is necessary to exclude the possibility of late brain abscess.

From the point of view of neurological function the results are satisfactory. There was no indication that application of the powder or installation of penicillin solution into the brain wounds caused any functional damage. Two of the earlier patients had headaches, with slight stiffness of the neck and positive Kernig sign, during penicillin treatment, and at the same time showed up to 1,000 red cells per c.mm. in the lumbar cerebrospinal fluid. At this period we were injecting as much as 12 c.c. of penicillin at a time, and as these symptoms of mild subarachnoid haemorrhage were not observed after the amounts injected had been reduced to 5 c.c. or less we concluded that they had been mechanically produced by repeated distension of the wound cavity.

No cases in this series showed any signs of meningitis after operation, nor was there any case in which the wound leaked cerebrospinal fluid.

The following are three examples of successful cases:

Case 15. On 14th July, 1943, mortar wound in right frontal region. He was not unconscious. On the same day operation was done in the forward area, "the wound excised and sutured, and depressed fragments of skull removed." On admission to No. 4 Mobile Neurosurgical Unit he was alert and rational. Slight papilloedema. Left facial weakness. His wound was bulging and its silkworm gut stitches were cutting out. X-rays showed indriven bone fragments and a large metal foreign body between the scalp and skull.

At operation on 20th July, six days after injury, the scalp wound was excised. The subcutaneous piece of metal was removed; the galea in contact with this was ulcerating and further scalp excision was necessary to remove this area. The bone defect (3 by 2 cm.) and dural defect (1.8 cm. diameter) were occupied by soft red granulation tissue and no brain substance was extruding. The brain beneath contained clot and 12 bone fragments over an area about 5 cm. in diameter. These were removed. Plastic procedure for scalp closure in two layers. Two tubes for penicillin.

Bacteriological examination showed in the skin edge clostridia, *staphylococcus* (not isolated) and "B. coli"; in the surrounding skin *Cl. tetani* in large numbers, "B. coli," and *B. pyocyaneus;* from the metal foreign body *B. pyocyaneus,* "B. coli" and clostridia.

Penicillin injections were carried out for four days, at first 5 c.c., then 3 c.c., then 2 c.c. into each tube. Before injection as much as 15 c.c. of thin brownish fluid could be aspirated (enterococci and "B. coli"). At the end of a week there was a slight gape over 1 in. at the centre of the radiating lines of the wound. From this area a penicillin-resistant *Staphylococcus aureus* was grown. Healing was almost complete by 19th August.

During the first days after operation the patient complained of headache, was at times drowsy, and he had slight weakness of his left hand, and slight dysarthria. Thereafter he made a satisfactory recovery, but in view of the presence of resistant staphylococci there is still a possibility of brain abscess.

Case 4. On 17th July, right frontal wound and compound fracture of the left tibia from aerial bomb. Unconscious for a few minutes. Both wounds excised and left open. Sulphanilamide applied to wounds. Sulphadiazine, 9 gm. intravenously.

20th July (No. 4 Neurosurgical Unit): Temperature 99.4°F. Pulse rate 92. Slight blurring of right optic disc. No other neurological signs. X-rays showed a right frontal bone defect (2.5 by 2 cm.) and fragments of loose bone in and beneath it.

Operation (Captain H. V. Slemon). When the skin had been excised and flaps reflected,

streaks of thick yellowish-white pus were seen beneath them. The bone defect was occupied by firm, healthy-looking clot. When this was removed a dural defect (2 cm. diameter) was exposed, which contained necrotic brain tissue and bone fragments. This was sucked away, leaving a cavity in the brain 4 cm. deep. The wound was frosted with penicillin-sulphanilamide powder and the scalp was closed in two layers, under some tension, in spite of plastic flaps, a tube being inserted for penicillin solution (25,000 units locally in five days).

Bacteriological examination showed in the subcutaneous pus *Staphylococcus aureus* and a few coliform organisms; in the clot and bone chips *Staphylococcus albus* (coagulase negative), "B. coli," and diphtheroids.

On 21st July his leg wound was explored and he was found to have spreading gangrenous cellulitis. He was given 315,000 units of sodium penicillin intramuscularly during $3\frac{1}{2}$ days.

For some days he had headaches, and was surly and taciturn. On the fifth day after operation his head wound gaped slightly at the centre and discharged pinkish pus for 8 to 9 days. On 3rd August he was for the first time alert and smiling. On 14th August his head wound showed complete and firm linear healing, he was free from symptoms and had no neurological signs. On 16th September he was reported as doing well.

Case 19. Injured 20th July in the occipital region by a mortar shell. Not unconscious, but blinded for 10 minutes. Sulphanilamide applied to the wound.

21st July: Wound excised and left open; sulphathiazole 4 gm., followed by 1 gm. four-hourly for six days.

27th July (No. 4 Neurosurgical Unit): Two open wounds (2.5 cm. and 1.5 cm. diameter) in left occipital region surmounted by a curved, sutured incision. Visual fields full to confrontation. Lumbar puncture; initial pressure 190 mm., yellow fluid. X-rays show an occipital bone defect, 5 cm. diameter, containing bone chips.

27th July: *Operation.* Free pus beneath the scalp. Brain fungus projecting through a dural opening (2 cm. diameter). Five bone chips removed from the brain to a depth of 2.5 cm. The resulting brain cavity held 5 c.c. of penicillin solution. Scalp closed in two layers by a plastic procedure. One tube for penicillin solution; 9,000 units in six days.

Bacteriological examination showed *Staphyloccus aureus* in swabs from all levels of the wound.

29th July: Fluid aspirated from the wound shows in films pus cells and no organisms; on culture *B. pyocyaneus.*

1st August: Wound edges moist at one point. On aspiration, 25 c.c. of thin blood-stained pus (culture: "B. coli," *B. pyocyaneus*).

3rd August: Culture of aspirated fluid—"B. coli," *B. pyocyaneus*, enterococci.

11th August: Wound intact. To Base.

27th August (No. 1 Neurosurgical Unit): Up and about. Wound soundly healed. No neurological signs. X-rays show that some bone fragments, indriven to a depth of 1.5 cm., remain. Cerebrospinal fluid normal.

16th September: Remains well.

In estimating wound healing not less than three weeks should elapse after operation before the scalp suture line over a brain wound can be regarded as completely healed by first intention. It is true that wounds which are going to break down at one or more points usually display warning signs —a moist rather than a dry wound, bulging of the wound, edema of the skin around it, and occasionally redness. But the fact remains that wounds noted on the medical history sheet as healed prior to the evacuation of the patient in the second week after operation have subsequently broken down. Our follow-up is not yet sufficiently complete to give the final results of healing, but it is probable that in six of the 20 survivors healing was by first

intention. In 13 cases the greater part of the wound healed by first intention, but part of it gaped or formed a sinus. In only one case was the gap sufficiently large to reveal brain tissue (brain fungus) and in this case the fungus was no more than one cm. in diameter (Case 21).

When the wound gaped it was usually where the tension was greatest: at the centre, or at the meeting-place of tripod wounds. The separation of wound edges was not more than a few millimetres, and the raw area was soon covered with epithelium. Sinus formation at one part of an otherwise healed wound was most commonly due to a dead space beneath it. This was particularly evident where the temporal muscle had been widely excised, or when part of the mastoid process had had to be removed. The dead space was also a problem in the healing of non-penetrating injuries, and, as Ascroft's work indicates (1943[1]), it is not peculiar to cases treated with penicillin.

TABLE II

COMPARISON WITH PREVIOUS RESULTS IN THE TREATMENT OF BRAIN WOUNDS

	Total	Completely closed	Left open	Died	Died of intracranial infection	Post-operative brain fungus
This Series—72 hrs. and older.....	23	22	1	3	2	1
Earlier Series (K.C. Eden)—72 hrs. and older.....	23	17	6	7	2	6
Sorgo (1942[3])—including 10 cases 72 hrs. and older.....	29	28*	1	13	10	?
Cushing (1918[2])—mostly less than 48 hrs. old.....	133	?	?	60	43	20†

* Closure of the dura by plastic operation. Scalp usually left open in all cases older than 24 hours.
† Details as to presence or absence of fungus available in only 92 cases.

Comparison with Earlier Series. In Table II this series of brain wounds is compared with earlier series. The figures are too small to be decisive, but they indicate the lines on which further data might be assembled. The incidence of fatal intracranial infection is probably as good an index as can be obtained of the efficiency of any treatment of brain wounds; total mortality rates vary widely with the distance of the neurosurgeon from the front line. It will be seen from Table II that in the last war about one-third of Cushing's brain injuries died of intracranial infection. In this war behind the German Army in Russia one-third of Sorgo's cases died of intracranial infection. In the present series from Sicily and an earlier series (K.C.E.) from the Western

Desert-Tunis battles the incidence of fatal intracranial infection was less than 1 in 10. In Eden's Western Desert series fewer wounds were closed and, even when wounds were closed, there was more post-operative brain fungus than in the present series. How much the improvement was due to the development of surgical technique with increasing experience of war surgery and how much to penicillin is difficult at present to estimate, but a number of the wounds in the present series were purulent and would not normally have been closed. From this preliminary use of penicillin we consider that the outlook for its further use in penetrating brain wounds, particularly as an aid to closure of old and infected wounds, is not unpromising.

GUNSHOT WOUNDS OF SCALP AND SKULL (NON-PENETRATING)

The frequency of pyogenic infection in non-penetrating gunshot wounds has already been noted as being much greater than in non-penetrating wounds due to blunt injury. In this series fracture of the skull also had a much greater incidence (Table I). It had been planned to run a parallel series of cases with sulphonamides, but in the event the wounds treated with sulphonamides were for the most part more favourable, in that they were smaller, cleaner, and less frequently associated with fracture of the skull. Cases arrived unexpectedly late and a considerable number of the wounds were so old and infected that from past experience no attempt would have been made to close them. They were closed with penicillin. The following is an example.

Case 40. Injured by rifle bullets in the head and right buttock on 20th July. Unconscious for one minute. Awoke to find his left arm completely paralysed. Prisoner of war for 11 days.

On admission on 4th August he had a wound 4 cm. long in the right parietal region, with rough bare bone at its base and discharging thick pus (Haemolytic streptococcus and *Staphylococcus aureus* on culture). Slight left facial weakness. Severe weakness and loss of position sense in distal part of left upper limb. At operation on 5th August (16 days after wounding) the wound was excised and the exposed bone, including depressed fragments of inner table, was removed. The dura was covered by granulations, but was intact. The wound was closed in two layers, a tube being inserted through a stab hole. Penicillin was injected through this tube twice daily for three days (total dose 3,000 units). Eight days after operation the wound was firm and dry, but there was a fluid collection beneath it. Five c.c. of thin, bloody fluid were aspirated which contained a few pus cells and coliform organisms and on culture yielded *B. pyocyaneus*. The wound remained firm.

When last seen three weeks after operation he was awaiting transfer to a convalescent depot. There was now only slight weakness, but still complete loss of postural sensibility, in the 3rd, 4th and 5th fingers of the left hand. The two small buttock wounds were clean and granulating.

The majority of cases were treated with a single application of penicillin-sulphanilamide powder at the time of suture. With this method there were two failures. One of these (Case 37) was doubtless due to the fact that in an 11-day-old wound the scalp was closed over bare and probably infected bone. Our experience suggests that nothing short of complete excision will deal effectively with exposed skull once it has been infected. In the other case (29) failure was unexpected, because, though the wound was infected

with *Staphylococcuss aureus*, it was only four days old and there was no fracture of the skull. The possibility arises that in this case bleeding during closure of the wound washed most of the powder out of the wound. After this experience bleeding was carefully stopped before closure, and more powder was insufflated before the last galea stitch was tied.

For wounds more than a week old penicillin solution was usually used for 3 to 5 days. Though the end result was satisfactory, and there was never any exacerbation of pre-existing infection as a result of closure, yet usually a sinus formed in some part of the wound and discharged pus for some days before it finally healed. This pus sometimes continued to contain gram-positive pyogens, an event which is so unusual during and immediately after penicillin treatment as to suggest loculated infection. In this connection it may be noted that, of the non-penetrating gunshot wounds treated with penicillin which were not associated with fracture of the skull, all except one (Case 29), healed by first intention; whereas of the 11 penicillin-treated wounds associated with fracture only four healed by first intention. Areas of osteomyelitis spreading from the site of fracture beyond the area of bone excision would certainly account for the behaviour of these wounds under penicillin treatment.

NON-PENETRATING WOUNDS DUE TO BLUNT INJURY

There were 23 cases in this group, the majority less than 24 hours old. Sixteen were treated with penicillin (all but one with a single application of powder), and seven were treated with a single application of sulphathiazole powder, supplemented in two cases by sulphonamides orally. In 22 cases healing was by first intention. The one exception was a very severe scalp wound with a central devitalised area of scalp three cm. in diameter, which had to be removed, and numerous radiating lacerations. This wound was completely closed after a prolonged plastic operation and insufflation of penicillin-sulphanilamide powder, but it subsequently gaped slightly over two cm. of its length, thereafter healing by granulation. The spreading of the wound may be ascribed to mechanical causes.

CONCLUSIONS

(1) Twenty-three cases of penetrating brain wound 3 to 12 days old were treated locally with calcium penicillin solution for 3 to 5 days after excision and suture. The average dose per case was 15,000 units. Three cases were also treated with parenteral penicillin because of associated fractures of long bones. Almost all the wounds were infected with gram-positive pyogens and 13 were to the naked eye purulent. Three patients died, two of them from intracranial infection. The remainder made a satisfactory recovery, as observed up to two months after operation. These results compare favourably with other published results, but the series is too small and has been observed for too short a time to enable conclusions to be drawn.

(2) Bacteriological examination of material aspirated from the brain

wounds showed that with penicillin gram-positive cocci disappeared from the wound within 48 hours in the majority of cases examined.

(3) Seventeen non-penetrating gunshot wounds of the scalp and skull up to 16 days old were excised and closed, and penicillin was applied in powder form, or subsequently injected. Wound healing was satisfactory (total or subtotal union) in all except two cases which broke down. The bacteriological behaviour of these wounds after penicillin was not as satisfactory as in the previous group: gram-positive cocci persisted in several cases. The persistence of purulent discharge containing gram-positive pyogens could be related to the presence of fracture, and it is suggested that persistence of gram-positive pyogenic infection was due to focal areas of osteomyelitis beyond the zone of excised skull, and beyond the influence of penicillin locally applied.

(4) In two of the 40 cases of gunshot wound of the head penicillin-resistant *Staphylococcus aureus* was encountered. The clinical course of these cases is so far satisfactory.

* * *

In Section 12 of the report (p. 27) the following summary of other wounds involving the nervous system is given.

* * *

Peripheral Nerve Injuries. In three cases in which wounds were closed (Cases 1, 10, 76) large peripheral nerves were found divided in the depths of the wound, and were sutured with fine silk. In two of these cases there was prompt linear healing of the skin wound. The third gaped in part, but subsequently healed. It is too early yet to assess the result on nerve healing.

Spinal Cord Injuries. In two back wounds a missile penetrated the spinal canal. In the first of these there was a cerebrospinal fluid leak through a wound infected with *Staphlococcus aureus* and *Proteus*. During a course of sodium penicillin intramuscularly this wound was excised and closed in layers. The leak ceased and the wound healed, partly by granulation, without any signs of meningitis.

In the second case a fragment of mortar bomb lodged in the cauda equina. On the second day the wound was excised in the forward area, treated with penicillin and sulphanilamide powder (5,000 units of penicillin per gm.) and left open. On the 7th day at Tripoli the wound, which looked clean, was closed with four layers of stitches. Unfortunately no cultures were taken. Fifteen days later this wound appeared perfectly healed.

REFERENCES

1. Ascroft, P. B. Treatment of head wounds due to missiles. Analysis of 500 cases. *Lancet*, 1943, *2:* 211–218.
2. Cushing, H. A study of a series of wounds involving the brain and its enveloping structures. *Brit. J. Surg.*, 1918, *5:* 558–684.
3. Sorgo, W. Über den primären Wundschluss bei der offenen Hirnverletzung. *Zbl. Neurochirurg.*, 1942, *7:* 73–109.

INTRACRANIAL DURAL CYST

WITH REPORT OF A CASE

CAPTAIN WEBB HAYMAKER, M.C., A.U.S., AND CAPTAIN MILES E. FOSTER, JR., M.C., A.U.S.

The Institute of Pathology of the Army Medical Museum, Washington, D. C., and the Station Hospital, Fort Leonard Wood, Missouri

(Received for publication April 7, 1944)

CYSTS LOCATED solely within the dura mater are a rarity. Apparently the only one on record was situated in the spinal canal. The case in point, described by Voss,[9] concerned a boy aged sixteen who over a period of about three months had developed symptoms of compression of the lower thoracic cord. Myelography disclosed subarachnoid block at the levels of the fifth and the eighth thoracic vertebrae. There was also a uniform dilatation of the spinal canal in this region. At operation a non-pulsating, pale cystic structure extending from the sixth to the tenth thoracic vertebra, was encountered. Incision of its dorsal wall released 8.0 cc. of clear fluid. Examination of the interior of the cyst revealed a smooth and glistening lining. No communication with either the subdural or the subarachnoid space could be found. When the ventral wall of the cyst was incised the dorsal part of the spinal cord could be clearly seen. Obviously, then, both walls of the cyst were dural. The incision in the ventral wall of the cyst was repaired and the entire dorsal wall was removed. Microscopic examination of the cyst wall disclosed "the usual fibrillary connective tissue" lined by a single layer of mesothelial cells.

On the other hand, some ten instances of cysts spatially related to the dura have been described (Elsberg, Dyke and Brewer,[1] Flatau and Sawicki,[2] Lehman,[3] Mixter,[5] Roger, Arnaud, Poursines and Alliez,[6] Schlesinger,[7] and Schmidt.[8]) All were intraspinal, most of them being situated in the thoracic region. Almost all were manifested by symptoms of cord compression. Dilatation of the spinal canal was the most conspicuous roentgenologic finding. The cysts lay snugly against the dorsal outer surface of the dura, to which in one or more places they were firmly attached. Almost all were single and unilocular. All contained colorless limpid fluid except for one into which a hemorrhage had occurred. In only three instances was there a communication between the cyst and the subarachnoid space, and this was by means of a narrow neck at the upper pole of the respective cysts.

The histologic appearance of the cyst walls varied somewhat. In about half the cases the wall was reminiscent of dura in that it was composed of rather dense interlacing connective tissue lined by a single layer of mesothelial cells. In two such instances a delicate trabecular connective-tissue network spanned the cyst cavity; in only one of these, that of Roger, Arnaud, Poursines and Alliez,[6] was there a free communication between cyst and subarachnoid space. Another type of wall had the appearance of hyperplastic

arachnoid in that it was composed of rather delicate loculated connective tissue, lined in places by flattened mesothelial cells.

Certain of the epidural cysts would seem to have originated as dural diverticuli, others as a herniation of the arachnoid through a congenital defect of the dura (see Elsberg, Dyke and Brewer[1] and Lehman[3]). Thus, they differ fundamentally from the intradural cyst described in the opening paragraph, as well as the intracranial cyst now to be considered.

CLINICAL HISTORY

First Admission to Hospital: 29 May 1942. Discharged on 3 June 1942.

Chief Complaint. Intense headache and a blurring of vision.

Present Illness. The patient, a male aged 34, an enlisted man in the Army and previously a steel worker, had had excruciating intermittent headaches and blurring of vision for two days prior to admission. The attack started suddenly soon after a verbal altercation with a superior officer. On questioning it was learned also that from the onset the patient had lost his sense of smell.

Previous Personal History. Other than typhoid fever in 1922 and three attacks of pneumonia (dates unknown), there had been no previous illnesses. As a child he was said to have fractured his skull when his head hit a radiator; no further history on this point could be obtained. He had had intermittent severe headaches since 1932. These occurred every two or three years. Over a period of a week or two they would reach a crescendo and then would disappear. During the bouts of headache there was usually a blurring of vision in the right eye but sometimes it was bilateral. Occasionally there was also pain in that eye.

Family History. Nothing of significance was elicited.

Physical Examination. The patient, of excellent physique, presented the picture of intense pain. He thrashed about the bed, pulled his hair and cried out. The temperature was 98.6°F., the pulse 84, the respirations 18, the blood pressure 128 systolic, 74 diastolic.

There was bilateral anosmia and a hemianesthesia of the left side regarded as of the "hysterical type." Otherwise the examination revealed nothing of note: speech and articulation were normal; the eyes moved freely in all directions; the pupils were equal, regular and responded to light and in accommodation; the Romberg test was negative; and reflex activity was unaltered.

Course. On admission the patient received morphia, $\frac{1}{4}$ grain subcutaneously, but it afforded little relief. A few hours later the pain over the head increased so that he tore at his hair and pounded on the walls. Later in the day he was given an intravenous injection of sodium amytal, $3\frac{3}{4}$ grains. Twice the injection had to be repeated. Over the next two days he received the drug by mouth. On 31 May 1942 he complained of severe pain in the right eye and because of restlessness had to be restrained. On the same day a spinal puncture was performed. The manometric figures were in the normal range. The fluid was not examined. On 1 June 1942, the third day after admission, the headache had disappeared. There is no further note on the progress of the anosmia. His improvement was ascribed to the therapeutic effects of strong suggestion while under the influence of sodium amytal. He was discharged from hospital 3 June 1942.

Readmission to Hospital: 12 July 1942. Date of Death, 26 August 1942.

Further Progress. The patient had been relatively well until 13 June 1942 when the headaches again appeared. Up to the time of readmission they had become progressively worse. During this time a blurring of vision of the right eye was very noticeable: it was "as if hair was hanging over that eye." There had been no vomiting, no vertigo, no difficulty in walking.

Physical Examination. The blood pressure was 125 systolic, and 90 diastolic, and the pulse rate was within normal limits. The reflexes were normally active. There was no defect of the sense of smell. The pupils were round and equal and reacted to light and in accommodation.

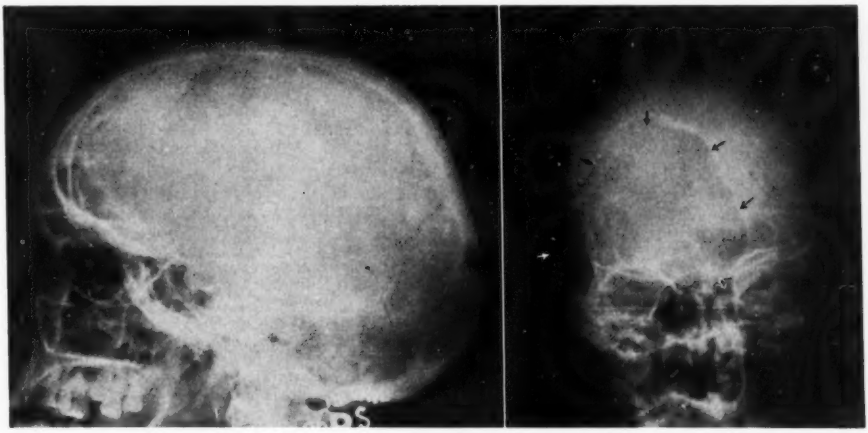


FIG. 1 (*left*). Roentgenogram of the skull from the right lateral aspect. The posterior cranial fossa is expanded and its calvarium considerably thinned. Adjacent diploic channels of the skull are dilated. Neg. 76573.

FIG. 2 (*right*). Antero-posterior plane. The edge of the bony defect is indicated by arrows. It will be noted that the calvarium in this region is uniformly thinned and that the edges of the defect are smooth. Neg. 79574.

Vo. D., 20/70; Vo. S., 20/40. Refraction: O.D., 20/20; O.S., 20/20 minus 1. Visual fields showed slight peripheral contraction but the blind spots were of the usual size. The fundi appeared normal. The headache and blurred vision were regarded as a consequence of refractive error.

Laboratory Findings. The routine studies, including Kahn, disclosed nothing of note.

Roentgenologic Findings. Films of the skull showed in the occipital region a uniform loss of bone substance measuring on the roentgenograms (which are somewhat magnified) 9×8 cm. The bony defect was bilateral but was more extensive on the right side. The margins of the defect were smooth and sharply delineated. In the immediate vicinity of the area of bone deficit the diploic channels appeared to be enlarged (Figs. 1 and 2). The roentgenologic diagnosis was that of an expanding lesion of the occipital bone.

Operation. A few days prior to operation the severity of the headache was such that it responded only to injections of morphia. Ergotamine tartrate was without benefit. Craniectomy was done on 27 July 1942, fifteen days after admission, the anesthetic consisting of 62 cc. of 5 per cent solution of sodium pentothal. By means of a high horseshoe cerebellar incision, the scalp was reflected over the expanded part of the occipital bone, all of which was posterior to the lambdoidal suture. A trephine opening was then made over what should have been the right occipital pole, but on removal of the bone a bluish pulsating membrane was encountered. It was incised and about 100 cc. of clear, colorless fluid was withdrawn. After enlarging the burr opening with a rongeur, thus making in the skull a window about 4 cm. in diameter, the impression was gained that the cystic structure occupied the entire right posterior cranial fossa. Since nothing of a neoplastic nature was encountered and since there was considerable distortion of all the venous sinuses, no further manipulations were carried out. The cranial defect was bridged by two vitallium Lane plates and closed in the usual manner, one plain Penrose drain being left *in situ*.

Fluid removed from the cyst had a specific gravity of 1.015 and contained 6.0 milligrams per cent of albumen. Tests for globulin were negative.

Subsequent Course. The patient returned to the ward in good condition. For the succeeding

three days, sulfanilamide, 1.0 gram every four hours, was given, and for another four days sulfathiazole in the same dosage. On the seventh post-operative day, at which time the level of sulfonamide in the blood was 1.4 mg. per cent, further use of the drug was discontinued. Altogether 38 gm. were administered.

On July 28th, one day after operation, the drain was removed from the wound; a small amount of serous fluid was noted on the dressing. On the same day the patient complained most of the time of nausea and on several occasions had projectile vomiting. On August 4th, most of the sutures were removed and a profuse drainage of serous fluid ensued. On the next day the patient complained of double vision. He became depressed, and at times confused. There was throbbing pain at the base of the skull as well as over the spinal column. On August 7th the remaining sutures were removed; the discharge from the wound was bloody.

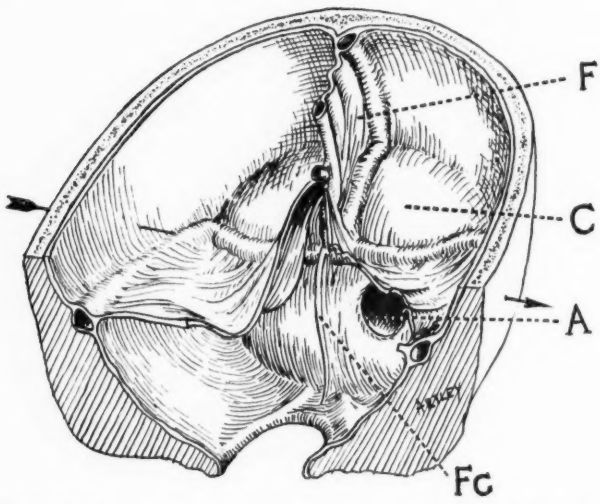


FIG. 3. Sketch of the posterior cranial fossa showing the position of the intradural cyst (*C*). The venous sinuses together with the falx cerebri (*F*), falx cerebelli (*Fc*) and tentorium are displaced anteriorly. The wall is intact except for an aperture (*A*) on the left side which is lateral to the falx cerebelli and beneath the lateral sinus.

On August 9th, after a probing of the wound with consequent escape of fluid, the pains and headaches were relieved. Off and on he complained of pains in the eyes. On August 19th he was allowed up in a wheelchair for ten minutes. Three days later there was an involuntary twitching of muscles, and protracted vomiting, mostly projectile, set in. At times the patient was irrational. Subsequently his temperature rose to 104.8° rectally, the pulse rate to 150, and respirations to 32. Death occurred on August 26th, thirty days after operation.

GROSS AUTOPSY FINDINGS*

General Inspection. Reflection of the scalp at the site of operation disclosed a considerable collection of pus between scalp and epicranium. Purulent material oozed from the edges of the vitallium plates which bridged the operative defect. Removal of the plates uncovered a cavity within the skull which contained about 100 cc. of greenish-yellow pus. The subtentorial part of the cranial cavity was somewhat enlarged. The brain was then removed. In shape and contour it was relatively normal except for a heavy yellowish exudate in the leptomeninges

* Army Medical Museum Accession 94853.

which was most marked at the base of the brain and which extended in diminishing degree on to the convex surface. Section revealed purulent fluid also in all parts of the ventricular system. Cultures yielded non-hemolytic staphlococcus aureus.

The Dural Lesion. The large cystic structure, unilocular and symmetrical, was found to be within the dura (Fig. 3). It measured 9.0 cm. from side to side, and 6.5 cm. antero-posteriorly. The posterior wall of the cyst lined the skull whereas the anterior wall bulged forward, displacing the tentorium and the falx together with their contained venous sinuses. The walls of the cyst, which varied between 2.0 and 3.0 mm. in thickness, were uniformly dense, tough and inelastic. The inner surface was covered unevenly by yellowish-brown granulation tissue coated by purulent exudate. The overlying venous sinuses were empty.

The dural wall was intact except beneath the tentorium on the left side where there was a spherical aperture which measured 3.0 cm. in diameter. Snugly herniated into the cyst through this aperture was a portion of the ansiform lobule of the cerebellum (Fig. 4). The

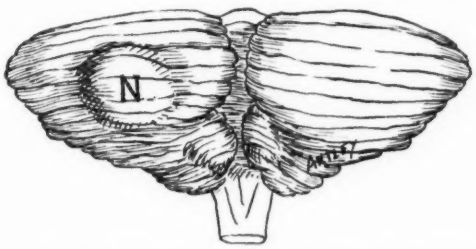


FIG. 4. Sketch of the cerebellum from the posterior aspect showing a nodule (*N*) of ansiform lobule which had herniated into the aperture shown in Fig. 3.

leptomeninges covering the protruded portion of the cerebellum were intact. At the periphery of the cerebellar protrusion the subarachnoid space appeared to be somewhat constricted.

MICROSCOPIC FINDINGS

The section illustrated in Figure 5 is taken through the cystic structure at the somewhat tangential coronal plane indicated by the arrow in Figure 3. Hence the section is composed of

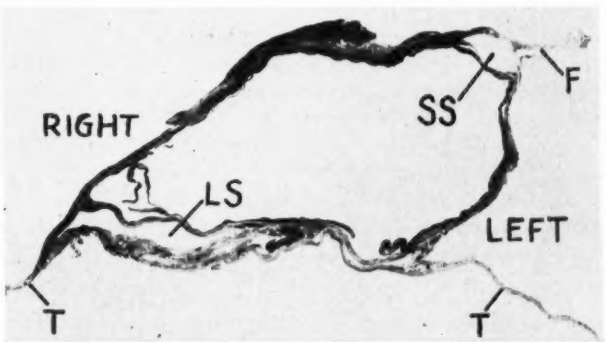


FIG. 5. A somewhat tangential coronal section through the cyst at a level indicated by the arrow in Fig. 3. The size of the cyst is somewhat reduced in the photograph. *F*, falx cerebri; *LS*, lateral sinus; *SS*, superior sagittal sinus; *T*, tentorium cerebelli. Hematoxylin and eosin stain. Neg. 78070.

superior, inferior and lateral portions of the cyst wall, as will be evident from the positions of the falx cerebri and the tentorium. Both the superior sagittal and the lateral venous sinuses are included in the section.

Microscopic examination of all parts of the cystic structure revealed a fairly uniform picture (Fig. 6). The wall was composed essentially of dense interlacing bands of fibrous tissue with well defined tissue channels. It was invaded to varying degree by inflammatory cells. Here and there, groups of histiocytes containing blood pigment were noted. In places the internal aspect of the wall was composed of granulation tissue. Coating the internal surface of the sac was a fibrino-purulent exudate. The walls of the venous sinuses were invaded by inflammatory cells but the lumina were patent.

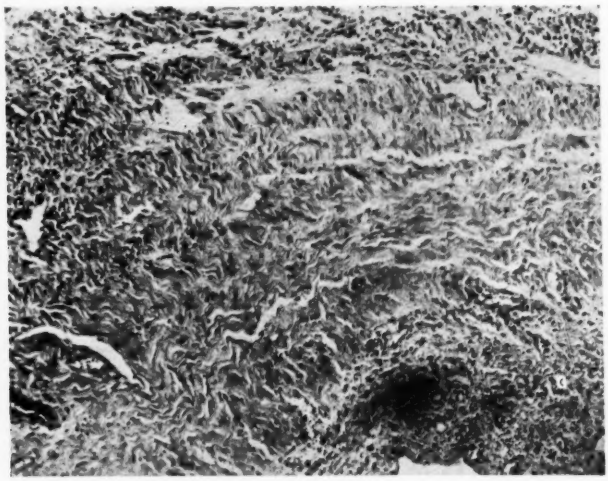


FIG. 6. A section from the posterior wall of the cyst. It shows typical dura containing tissue channels. The inner surface of the cyst (below) is coated by granulation tissue whereas the outer portion (above) contains a sprinkling of inflammatory cells. Hematoxylin and eosin stain. ×60. Neg. 78065.

Sections of the cerebellum through the portion which had herniated into the cyst failed to reveal parenchymal changes. The leptomeninges in this region were intact and the arachnoid space contained moderate numbers of inflammatory cells. No evidence of undue pressure on leptomeninges at the periphery of the herniated portion of the cerebellum could be found.

Examination of the brain confirmed the gross impression of purulent leptomeningitis and ependymitis. The only other finding of significance was that of an acute ulcer of the duodenum, fairly deep and 1.0 cm. in diameter.

DISCUSSION

Histologic examination of various parts of the cyst wall, posterior as well as anterior, revealed the unmistakable pattern of dura. Even at sites where the infective process was most marked the dura was of uniform thickness. The fact that the part of the wall applied to the skull lacked no feature of normal dura would seem to rule out the possibility that the lesion may represent the end stage of an epidural hemorrhage which had been overgrown externally by collagenous connective tissue, with subsequent absorption of

the blood and replacement by fluid. The phagocytosed blood pigment in certain parts of the cyst wall are to be ascribed to hemorrhage from the newly formed granulation tissue rather than to ancient hemorrhage.

It seems reasonable to ascribe formation of the cyst to a failure of fusion of the two layers of the dura, which ordinarily unite at the end of the second month of fetal life. Since from a developmental standpoint the two dural layers split to enclose the venous sinuses, one would have expected that with the advancing cleavage of the two dural layers a sinus would have been penetrated. The failure of this to occur suggests that the plane of cleavage had shifted from between the two dural layers to the inner part of the wall of the outer layer as the venous sinuses were approached.

The mode of formation of the fluid is not clear but obviously it gradually increased in quantity, first becoming clinically manifest some ten years before death. It is presumed that the intracystic tension gradually thinned that part of the cyst wall beneath the left lateral sinus, causing an aperture to form. And it seems reasonable to suppose that during the long symptom-free intervals the fluid may have had access to the subdural space, and that as the cyst increased more in size, the aperture became sufficiently plugged by cerebellum to prevent further escape of fluid. That the plugging of the aperture was relatively recent would seem to be borne out by the lack of changes in leptomeninges and cerebellar folia at the site of the annular compression. The destruction of the inner table of occipital bone overlying the cyst may be ascribed to transmission by the fluid of intracranial arterial pulsations to the endocranium. The occurrence of such pulsations had been noted at the time of operation.

Certain malformations of the dura in the posterior cranial fossa, e.g., a doubling of the falx cerebelli, have been described (Iso[4]) but no intracranial lesion similar to the one in point has come to the writers' attention. Apparently the only other intradural cyst on record is that in the spinal canal described by Voss, cited in the foregoing. In this case too the cyst steadily increased in size, bulging the spinal canal and giving rise to signs of cord compression. The same capacity to collect more and more fluid was manifested also by the above-cited epidural cysts.

SUMMARY

A case of a large intradural cyst in the posterior cranial fossa is presented. There was marked erosion of the occipital bone overlying the cyst. Symptoms, consisting of headache and blurring of vision of the right eye, occurred intermittently over a period of ten years. It is suggested that formation of the cyst is to be ascribed to a failure of union of the two layers of dura during fetal life.

REFERENCES

1. Elsberg, C. A., Dyke, C. G., and Brewer, E. D. The symptoms and diagnosis of extradural cysts. *Bull. neurol. Inst. N. Y.*, 1934, *3*: 395–417.
2. Flatau, E., and Sawicki, B. Kyste hémorragique intradural du sac spinal. *Rev. neurol.*, 1924, *2*: 589–596.

3. Lehman, E. P. Spinal extradural cysts. *Amer. J. Surg.*, 1935, *28:* 307–322.
4. Iso, M. Seltene Abnormalitäten an der harten Hirnhaut des Menschen. *Folia anat. Japon.*, 1939, *18:* 407–412.
5. Mixter, W. J. Spinal column and spinal cord. In: *Lewis' Practice of Surgery.* Hagerstown, Md.: W. F. Prior Co., Inc., 1943, *12:* Chap. III, 63–65.
6. Roger, H., Arnaud, M., Poursines, Y., and Alliez, J. Kyste intradural dorsal communiquant avec le liquide céphalo-rachidien. Image lipiodolée en goutte pendante. Guérison opératoire de la compression médullaire. *Rev. neurol.*, 1933, *40:* 1155–1163.
7. Schlesinger, H. Beiträge zur Klinik der Rückenmarks- und Wirbeltumoren. *Jena: G. Fischer*, 1898, 208 pp.
8. Schmidt, A. Cyste der Dura mater spinalis, einen extramedullärem Tumor vortäuschend, mit Erfolg operiert. *Dtsch. Z. Nervenheilk.*, 1904, *26:* 318–323.
9. Voss, O. Rückenmarkskompression durch eine intradurale Cyste. *Dtsch. Z. Chir.*, 1936, *248:* 341–345.

SUTURELESS REUNION OF SEVERED NERVES WITH ELASTIC CUFFS OF TANTALUM*

PAUL WEISS, PH.D.
Department of Zoology, University of Chicago, Chicago, Illinois

(Received for publication April 14, 1944)

THE ADVANTAGES of using closely fitting sleeves as links between severed nerve stumps have been described previously.[5,6,7] The sleeves consisted of segments of artery, either fresh or frozen-dried and rehydrated. The experimental material on which the conclusions regarding the merits of the method were based included nearly 700 nerve unions in various animals (rat, over 500; rabbit, 21; fowl, 37; cat, 30; monkey, 81). Analytical studies of the healing and regeneration of nerves following sutureless splicing with arterial sleeves have demonstrated that the salient features to which this method owes its superiority are the following:[7]

(1) *Absence of Sutures.* This permits longitudinal traction to be transmitted directly from stump to stump through the tissue filling the gap, whereby the latter becomes converted into a system of parallel guide rails of strictly longitudinal orientation, over which the regenerating nerve fibers, sheath cells and blood vessels are then conducted into the distal stump without extensive branching, straying or confusion. The same longitudinal stresses turn invading connective tissue into an innocuous longitudinal course along the surface, thus preventing penetration of scar tissue into the space between the nerve stumps. Moreover, foreign body reactions, disorienting tissue whorls, and similar contingencies of sutures are precluded.

(2) *Confinement of Fluid.* A proper degree of liquidity of the tissue uniting the nerve stumps is prerequisite for nerve regeneration of optimal density. Liquid accumulates in the gap as a result of hemolysis, fibrinolysis, exudation from the nerve, and perhaps vascular transudation. The sleeve serves to prevent its dissipation.

(3) *Insulation and Protection.* The sleeve prevents adhesion between the nerve junction and the surrounding tissue, protecting the nerve against invasion by fibrous tissue and precluding the escape of nerve fibers.

Arterial sleeve-splicing shares feature (1) with the method of plasma suture,[4,8] feature (3) with many past and current procedures of nerve wrapping, but is unique in the combination of functions it serves.

It has been evident throughout this work that the clinical application

* The research reported in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Chicago. It was aided by the Dr. Wallace C. and Clara Abbott Memorial Fund of the University of Chicago.

Courtesies of Dr. K. S. Lashley, Director of the Yerkes Laboratories of Primate Biology at Orange Park, Florida, in providing the facilities for the monkey experiments; technical assistance by Dr. R. W. Sperry; and the courtesy of the Tantalum Defense Corporation in furnishing the test material are gratefully acknowledged.

of the principle of sutureless sleeve-splicing would be greatly facilitated if sleeves could be made from a material with physical and physiological characteristics similar to arteries, but more readily procurable. The success reported with the shielding of suture lines by tantalum foil[3] suggested that this material might be adaptable for the purpose.* This proved to be the case, as is illustrated in the following account.

METHOD

The problem was primarily a technological one, namely, to fashion tantalum foil into elastic cuffs of the caliber of nerves. Ordinary tantalum foil is highly pliable and unelastic. Unprotected exposure to heat makes it brittle. Yet, after some experimentation a heat treatment was finally discovered by which the foil could be molded into cylindrical rolls of the desired shape and resilience. The best results thus far have been obtained by the following procedure.

Tantalum foil, 0.00025 to 0.0005 inches thick, is wrapped around a cylindrical core which is to serve as heat conductor. The core consists of a central steel rod over which a fitting jacket of glass tubing is pulled. For each size of sleeve a matching size of core is used. The measurements of the foil are so chosen that it will cover two turns when rolled over the glass cylinder. Thin wire is wound around the tightly wrapped foil to keep it in place. The whole unit is then placed into an electric furnace for a specified period, the length of which varies with temperature, thickness of the foil, dimensions of the core and thermal properties of the latter, and must be determined empirically. A few seconds may decide the difference between success or failure. Underexposure leaves the foil unelastic, overexposure renders it brittle and useless. It will be noted that the inside of the foil is in contact with a heat conductor, while the outside is exposed to the radiant heat of the furnace.

When properly treated, the foil emerges from the treatment with changed properties. It has assumed the shape of a cylindrical coil of approximately the diameter of the core, has lost its pliability and instead become highly elastic. Owing to the fact that the outer turn has shielded the inner turn against direct heat radiation, the former turns out harder and more resilient than the latter. This gives the cylinder self-sealing capacity, inasmuch as the outer edge presses downward against the underlying turn, while the inner edge presses outward against the overlying turn. This asymmetry explains the fact that such a roll when forcibly uncoiled and allowed to recoil assumes the shape of an open spiral. To return it to its cylindrical shape, the originally inner edge must be tucked under the more highly curved outer turn. Each sleeve is to be allowed about one-half turn of overlap in its final form. This is achieved by trimming the outer edge.

Such sleeves are not only perfectly elastic, but have considerable structural strength. For instance, a tube, 27 mm. long and 3 mm. wide, made from foil 0.01 mm. thick, is able to withstand compression in the direction of its longitudinal axis up to 2000 g. without collapsing. After lateral compression by 700 g. pressure, it still resumes fully its cylindrical shape.

The sleeves must be chemically clean, for impurities along their surface would provoke tissue reactions.

In using these sleeves for the joining of nerve stumps or for junctions between nerve stumps and grafts, it has proved more convenient to treat them as tubes in the manner previously described for arteries, rather than by uncoiling and recoiling. One may use either a modification of the arterial splicing clutch[6] or adopt the following simplified procedure.

A bevelled thin-walled metal or glass canula, slightly wider than the nerve stump, is at-

---

* I owe my acquaintance with this material to Major W. P. Van Wagenen, M.C., A.U.S.

tached to a saline-filled syringe. The sleeve, slightly distended, is pulled over the canula. The nerve end is placed on the bevel, eased into the orifice, and finally sucked farther in by raising the plunger of the syringe. The sleeve can then be easily slipped from the canula onto the nerve stump, whereupon the nerve end is extruded from the canula by depressing the plunger. An air aspirator may be used in place of the syringe.

In the absence of special equipment, any hollow cone wide enough at its base to hold the nerve stump can be used as an aid in sliding the metal sleeve over. The width of the sleeve should be so chosen that it will fit the nerve closely without tightness. Elasticity and overlap allow for adjustment to local conditions. The length of the sleeve will vary with the requirements of the individual case, particularly the location of the lesion and the extent of nerve adhesions.

The actual linking of nerve stumps which can be approximated to within several millimeters is done as follows. The sleeve which is to serve as link is pulled to full length over the distal stump. In order to facilitate handling of the proximal stump, a shorter tantalum cuff of corresponding diameter is pulled over the proximal end, its rim flush with the cut surface. The longer sleeve is then pulled back from the distal stump and telescoped over the cuffed end of the proximal stump, as in the joining of two stovepipe segments. The grip of the sleeve on the nerve ends may then be tightened by a gentle wrapping movement or by a loop of silk drawn around it and left in place until coagulating blood which has seeped between the overlapping edges has sealed the tube. No further means of attachment are necessary if the sleeve is of sufficient length. Nerve ends in a well-fitting sleeve act like pistons, and the suction which their separation creates tends to hold them in place. The fact that moderate tension can thus be tolerated without risk of rupture of the link, is a major factor in the success of the ensuing regeneration process.

A gap of several millimeters between the nerve ends has been found quite acceptable. The maximum tolerable length compatible with good regeneration remains to be determined. Where force becomes necessary to bring the nerve ends within range, it should not be applied at the ends or within the sleeve, but at more remote levels; for instance, by a sling stitch of tantalum wire looped through both stumps well above and below the sleeve region. This loop should take up only the excess of stress, but must not be shortened to a degree where it would leave the nerve ends in between slack.

Spider monkeys and cats were used for the experiments. Peroneal and tibial nerves severed in midthigh were reunited with tantalum sleeves. The animals received only a thin coat of synthetic resin over the skin suture, but neither casts nor splints. Their movements were in no way restricted. Eight nerve unions were performed in monkeys, and twelve in cats.

RESULTS

Five monkey and six cat unions have thus far been examined, the oldest seven weeks after the operation. In none of them had the nerve stumps pulled loose in spite of the unrestrained exercise of the animals from the very first day after the operation. Only in two of the earliest cases had the sleeves crumbled, evidently owing to inexpert handling. In all other cases, the sleeves had remained unchanged.

There were no or only very slight adhesions between the nerve and the wound bed. A continuous fibrous nerve sheath was present. After its dissection the tantalum sleeve, covered by a very thin, smooth, transparent membrane, came into view. The ends of each sleeve had become walled off by rings of connective tissue continuous with the epineurium, undoubtedly due to the chronic irritation set up by the sharp rims. However, since these scars formed at a safe distance from the nerve gap, did not penetrate into the

nerve, and had not given rise, at least not at this stage, to lateral adhesions, they do not seem to present a serious hazard. After slitting the thin cover membrane, the sleeve was grasped by its overlapping edge and stripped off, or rather unwound, from the nerve. It had lost none of its resilience. Its surface was slippery, apparently from serous fluid.

FIG. 1. Peroneal nerve of spider monkey, 5 weeks after sutureless reunion of the stumps (gap 4 mm.) with tantalum cuff. The cuff has been removed. Its former site is indicated by a white rule, the dotted part of which shows the extent of the original gap. Proximo-distal direction from top to bottom. ×3.

Removal of the sleeve bared the surface of the nerve junction. As early as five days post operative, the nerve ends were found reconnected by a cylindrical sheath which had grown along the inside of the sleeve. The interior was still highly fluid. At five and seven weeks post operative, the connection was firm. Except for its greater transparency, the level of the former gap could not be distinguished. The nerve in this region offered the aspect of a continuous cylinder (Fig. 1) with a perfectly smooth glossy surface without a trace of scar tissue or other unfavorable reaction against the metal.* The fact that the nerve can thus slide freely in the sleeve, constitutes one feature in which the tantalum cuff is superior to frozen-dried arteries, in which local adhesions of the nerve to the inner wall of the sleeve are not uncommon.

The microscopic picture bears out the macroscopic appearance of perfect reunion. Figure 2 illustrates the junction of a peroneal nerve as it appeared after the removal of the cuff without further trimming of the surface. One notes that no foreign body reaction or perineurial scar formation has occurred anywhere within the sleeve. For the rest, the picture speaks for itself. Specifically, the following points describe the character of the union.

(1) The gap has become bridged by a tissue which proceeded to form an integral link between the stumps, rather than merely a cementing scar.

(2) Sheath cell cords and nerve fibers have passed in straight parallel alignment through the gap into the distal stump and straight on down the latter.

(3) There is no profuse branching, straying and commingling of fibers at the level of the union.

* Concerning the indifference of tissues to tantalum, see Burke,[1] and Pudenz and Odom.[2]

(4) There has been no ingrowth into the junction of cicatricial connective tissue. All endoneurial and perineurial connective tissue has likewise been turned into a strictly longitudinal course, where it cannot impede nerve fiber growth.

(5) High liquid content of the tissue forming the junction has been preserved. This can be told directly from the loose texture of the tissue and also from its greater shrinkage during fixation, which gives it a "waistline" appearance. In spite of the abundance of liquid channels, the mechanical firmness of the link is assured by the tensile strength of the longitudinal strands of endoneurial fibers serving as ties.[7]

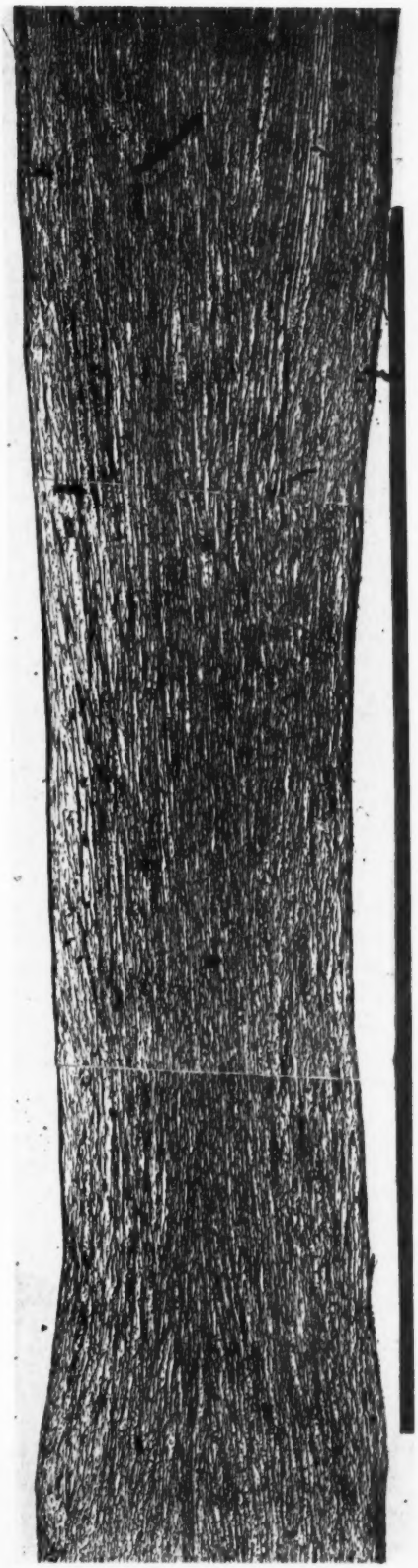


FIG. 2. Photomicrograph of a longitudinal section of the same nerve as in Figure 1. Silver impregnation after Bodian. The extent of the original gap between the stumps is indicated by the black rule on the margin. Note that the old perineurium of the stumps ends at the levels of the original cut surfaces, thus marking the limits of the former gap. Proximo-distal direction from top to bottom. ×43.

(6) No local edemas, neuromas or gliomas have formed.

(7) Since the nerve fibers, in passing from the proximal to the distal stump, maintain a steady straight course, they will restore a more orderly pattern of connections between the centers and the periphery than would otherwise be possible. This may have an important bearing on functional recovery.[6]

(8) Vascularization of the junction has been ample. The main vessels have grown straight through, following the general longitudinal di-

rection, and have supplied the whole region with a network of capillaries. In fact, this vascular supply from the intraneural sources is so abundant that it makes the recurrent warnings against the wrapping of suture lines, on the grounds that such procedures prevent extraneural vessels from penetrating, appear wholly unwarranted.

Rate of axon downgrowth has not yet been established. After 5 weeks, the peripheral stump was densely populated with regenerated axons at a level 20 mm. beyond the original cut surface. There is no record of just how much farther they had advanced, except that they had not yet reached the next distal sample level, 55 mm. from the cut. The whole picture, however, is such that the later outcome can be predicted on the basis of past experience with many hundreds of nerve unions studied both histologically and functionally. Unions such as the ones described here will lead to prompt and full reinnervation of the periphery, free from the impeding and delaying effects of intraneural fibrosis. In view of the predictability of the outcome, presentation of the results in this early phase has seemed justified. The functional results will be reported at a later date.

The two cases mentioned above, in which the sleeves had become buckled up, were total failures. Holes had formed at the dents and scar tissue had penetrated freely through these openings. The interior was filled with a bloody soft mass, evidently a residue of repeated hemorrhages. Except for a few strands along undamaged parts of the sleeve wall, there was no firm connection between the stumps. The proximal stump ended in a neuroma. The failure of effective reunion was so patent that no histological study was made. Creased and dented sleeves are obviously a potential source of injury and irritation to the nerve. However, no further mishaps of this kind have occurred since those early accidents. Yet, it is well to keep in mind that the danger of such an occurrence would increase in the vicinity of a joint, calling for protective measures such as temporary fixation.

The contrast between the successful and unsuccessful cases makes it clear that the question of the merit of using tantalum—or any other material, for that matter—in the repair of nerves, cannot be answered in a general way. Much depends on how the material is being used. If used properly, tantalum sleeves seem to perform very adequately as links between unsutured nerve stumps.

The obvious limitation, that they are applicable to straightway unions only and would be unsuitable where nerves are subject to bending, e.g., at a joint, might in some cases be overcome by leaving the sleeve in place only just long enough to permit firm reunion of the stumps and the formation of a new nerve sheath, while the joint is in fixation, and then reoperating for removal of the cuff, which can be easily pulled out in one piece, with a single move, without danger to the nerve or its circulation. But there will undoubtedly remain certain classes of lesions in which the use of rigid sleeves will be impracticable.

Aside from the excellent frame they provide for nerve regeneration,

tantalum sleeves simplify the technique of nerve union considerably, and thus save time. Moreover, they can be easily applied to nerves of even the smallest caliber which would defy neat end-to-end suture.

SUMMARY

A method is described by which tantalum foil can be fashioned into resilient self-sealing tubes, which may be used as cuffs for the sutureless linking of severed nerve stumps in the manner previously described for arterial sleeves.

Preliminary observations on monkey and cat nerves joined by this method have demonstrated that excellent reunion between the stumps with the properties required for optimal nerve regeneration may be achieved if the sleeves have been suitably shaped and properly handled.

REFERENCES

1. Burke, G. L. The corrosion of metals in tissues; and an introduction to tantalum. *Canad. med. Ass. J.*, 1940, *43:* 125–128.
2. Pudenz, R. H., and Odom, G. L. Meningocerebral adhesions. *Surgery*, 1942, *12:* 318–344.
3. Spurling, R. G. The use of tantalum wire and foil in the repair of peripheral nerves. *Surg. Clin. N. Amer.*, 1943, *23:* 1491–1504.
4. Tarlov, I. M., and Benjamin, B. Autologous plasma clot suture of nerves. *Science*, 1942, *95:* 258.
5. Weiss, P. Nerve regeneration in the rat following tubular splicing of severed nerves. *Arch. Surg., Chicago*, 1943, *46:* 525–547.
6. Weiss, P. Nerve reunion with sleeves of frozen-dried artery in rabbits, cats and monkeys. *Proc. Soc. exp. Biol., N. Y.*, 1943, *54:* 274–277.
7. Weiss, P., and Taylor, A. C. Histomechanical analysis of nerve reunion in the rat after tubular splicing. *Arch. Surg., Chicago*, 1943, *47:* 419–447.
8. Young, J. Z., and Medawar, P. B. Fibrin suture of peripheral nerves. *Lancet*, 1940, *2:* 126–128.

REPAIR OF CRANIAL DEFECTS WITH TANTALUM

MAJOR ROBERT C. L. ROBERTSON, M.C., A.U.S.
Brooke General Hospital, Fort Sam Houston, Texas

(Received for publication February 13, 1944)

AUTOGENOUS bone transplant repair of cranial defects is not completely satisfactory. It entails an extended or separate operative procedure to secure bone, the size and contour of which leaves something to be desired. A "crows-nest" appearance may result from a multiple fragment repair and there is some question of the survival of the bone fragments as osseous tissue. An ideal substitute material has yet to be discovered. Such a substance should be readily available, easily worked, preferably workable when cold, strong enough to withstand ordinary trauma, and above all, inert in tissue.

Until 1936, when Venable, Stuck and Beach[8] found that vitallium caused no tissue reaction, a satisfactory substitute for bone was unavailable. In the search for an inert metal, Burch (1938) obtained tantalum* and, for the first time, used it in surgery.[1] Burch and Carney's observations on the inertia of tantalum in tissues were reported in 1942.[3] Burke (1940) reported that no reaction was produced by tantalum wire in soft tissue.[2]

The adaptability of tantalum to neurosurgery was demonstrated by Pudenz (1942)[6,7]. He proved that brain substance and meninges of cats tolerated the metal extremely well and that the skull plate replacements were efficient. Fulcher (1943)[4] reported a case in which he repaired a frontal skull defect with tantalum sheet metal. Neither Craig nor Spurling have reported their considerable experiences with tantalum in several applications in the field of neurosurgery.†

Some information regarding tantalum will explain its suitability for use in surgery, and particularly in cranioplasty. It is an element; a heavy metal with a density of 16.6 (about twice that of steel). It reacts only to strong alkalies, hydrofluoric acid, and concentrated or fuming sulfuric acid at ordinary temperatures. It is virtually non-magnetic and is very high in the EMF Series[5]. These attributes obviate the "storage-battery effect" frequently found in alloys when placed in tissues. Its chemical inertia obviates reactions to body fluids.

Tantalum is workable when cold but cannot be cast. Strength and thermal conductivity are approximately that of steel. The coefficient of expansion of tantalum is 50 per cent that of steel, 40 per cent that of copper and 30 per cent that of silver[5]. Its workability makes it "adaptable to the situation" in contrast to stock or specially cast metal replacements. In the range of body temperature, changes in size of the metal are insignificant.

* Tantalum is produced by the Fansteel Metallurgical Corporation, North Chicago, Illinois.

† While the present article was in press the use of tantalum wire and foil in peripheral nerve surgery was reported by Lt. Col. R. G. Spurling (*J. Neurosurg.*, 1944, *1*: 133–148).

Tantalum sheet metal (.015 and .02 inches thick) has been used to repair skull defects at Brooke General Hospital, Fort Sam Houston, Texas, since September, 1942. It has been found that tantalum is easy to use, very adaptable to situations met at the operating table and it has been demonstrated that its reaction in tissue is minimal. No reaction was observed in one tantalum cranioplasty revised after six days, or to segments of tantalum foil after being in place over cortical lacerations so long as 54 days.

Two methods of cranioplasty with tantalum have been used at Brooke General Hospital. One is a two-stage operation, the other a one-stage procedure. In the former, the bed for the plate is prepared by mortising the periphery of the bone defect. A shelf is made in the outer table by chisel, or burr, 2 to 3 mm. beyond the limit of the defect. An impression of the defect, and details of the margin of bone, is obtained with ordinary dental impression compound. A wax model is made duplicating the contour of the portion of the skull to be replaced. From this positive, a die and counter die are made of either calcar, or zinc and lead to swage the metal to conform to size, shape and contour of the missing bone. At secondary operation, the plate is merely placed into the previously prepared bed and fixed in position.

The more frequent, and highly satisfactory method, is a one-stage procedure. The bed is prepared as described above. The approximate size segment of tantalum is molded by bending and shaping, or more frequently by "beating" to contour. Then the exact outline is cut with heavy scissors to conform to the outline of the mortised defect. By this method, done at primary operation, it has been possible in several of the cases to omit the precaution of fixing the plate into position.

If the outline has been cut accurately to size and shape, after the contour has been formed, one border of the plate is engaged into the shoulder of the mortise and by slight bending, and forcing the opposite border into its corresponding shoulder, the plate will fit so well when it has flattened out as a result of its inherent spring, that it will lock itself into position. This is not so difficult as it would seem in description.

Other methods exist or may occur to the surgeon. Moulage, or other type of impression, can be made of the cranial defect before operation. Contour and approximate size and shape of the replacement can thus be formed preoperatively. This planned type of replacement is advantageous, especially in the frontal regions of the skull where bilateral exact symmetry is most important.

Fixation of the tantalum replacement may be accomplished by wire suture passing through the edge of the plate and through the adjacent bone. In several instances, we used small triangular trimmings of the tantalum sheet, utilizing the principle of glazier's points. These points are driven into the diploic space about the margin of the defect in the same manner that a glazier immobilizes a glass window pane before applying putty about its border. We believe that, with rare exceptions, all replacements should be fixed and the "glazier point" method has mechanical advantages over fixation with wire.

The two-stage operation may be preferable where a prolonged one-stage procedure is contraindicated or in those portions of the skull where the curvature is great, such as over the occipital pole, or where there are complicated contours such as the inferior fronto-temporal-parietal area. Preoperative preparation of the plate is preferable in the latter.

A series of 26 cases of tantalum cranioplasty in service men has been done. All cases have been gratifying in the ease with which the cranial repair has been made, the efficiency of the repair and the cosmetic results. Four illustrative cases are reported in some detail. Although the reports may not

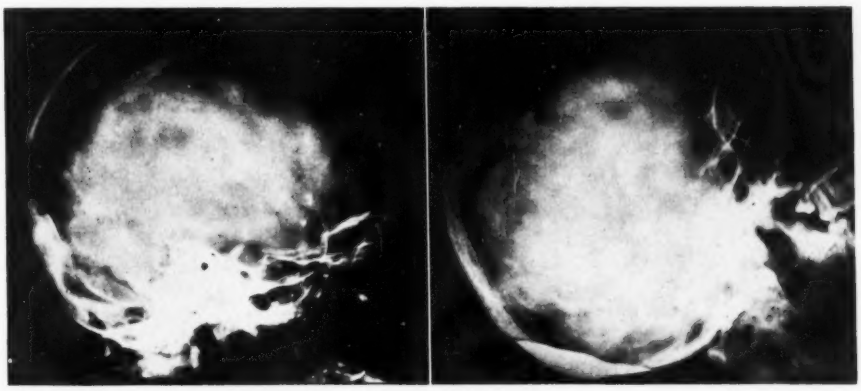


FIG. 1 (*left*). Case 1. Preoperative film showing depressed fracture, occipital region.

FIG. 2 (*right*). Case 1. Postoperative film showing result of two-stage cranioplasty. Note slight, but insignificant anterior dislocation of tantalum replacement.

reflect a constant refinement in technic, practice has, naturally, resulted in many minor changes in our original methods.

CASE REPORTS

Case 1. D.A., Brooke General Hospital.

Skull Pathology. Depressed fracture, occipital region, midline.

Associated Injuries. Multiple scalp lacerations, fracture of inferior pubic ramus, moderate concussion (unconscious 24 hours).

Mode of Injury. After having skidded and fallen with a motorcycle, he was struck by a heavy combat vehicle, January 8, 1942.

Course and Residuals. Transient, homonymous hemianopia, right. Relatively uneventful recovery. Returned to duty in a few weeks. Later developed headaches and dizziness precipitated by sunlight and activity for which he was hospitalized three times. Readmitted on August 31, 1942 and transferred to Brooke General Hospital September 16, 1942.

Operation. First stage, September 28, 1942: Removal of depressed area of skull, 6 × 7 cm. diameter and of approximately 3 cm. depth, the external occipital protruberance being the vortex of the cone-shaped depression. Dura was intact. The edges of the bone defect were mortised. An impression of the defect and bone edge was made with dental impression compound. The dental service swaged a segment of tantalum, reproducing a normal contour of this portion of the skull, of exact size and shape of the bone defect. *Second stage,* October 31, 1942: The tantalum replacement was introduced and anchored to bone with two tantalum wire sutures.

Postoperative Course. Uneventful recovery. Returned to full field duty, December 23, 1942.

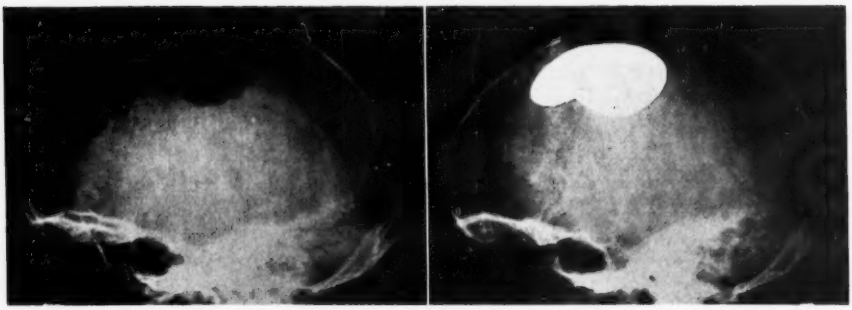


FIG. 3 (*left*). Case 9. Lateral skull film showing defect resulting from debridement (another hospital) following airplane crash.

FIG. 4 (*right*). Case 9. Film after single-stage cranioplasty. This plate was not fixed in place at operation since it locked itself in position so firmly.

Case 9. M.N.C., Brooke General Hospital.

Skull Pathology. Skull defect 4.5 × 6.7 cm., left parietal.

Associated Injuries. None on admission to Brooke General Hospital.

Mode of Injury. January 24, 1943, in a forced landing crash, his airplane struck a tree and he sustained a depressed fracture of the left parietal region and lacerations about the head and face.

Course and Residuals. He was not unconscious but was aphasic. There was weakness of the right hand, paralysis of the right thumb, hypaesthesia and hypalgesia of the right hand. A debridement and repair of scalp and facial wounds was done shortly following the accident. On the following day, the depressed fragments of skull were removed. Since dura was intact, it was not opened for investigation of the cortex. Aphasia improved rapidly and the paresis and sensory changes of the hand only slightly less rapidly. He was later transferred to Brooke General Hospital.

Operation. On March 23, 1943 the three-limb scar of the previous operation was completely resected down to periosteum. The galea was separated from periosteum over the bone defect. The periosteum was incised near the margin of the defect and turned down as a flap.

A mortise was created in the border of the defect. A tantalum replacement was molded and trimmed to exactly fit the mortise. On increasing the curvature of the plate slightly, while forcing it into the mortise, it locked itself into position so that it could not be displaced. No fixation was thought indicated. The wound was closed anatomically.

Postoperative Course. He was out of bed the following day for a short walk on the hospital grounds. On the second day he went for an extended walk. Daily needle aspirations of fluid and blood from beneath the scalp flap were necessary for a time. He was returned to full field duty April 10, 1943.

Case 10. S.C.N., Brooke General Hospital.

Skull Pathology. Compound comminuted depressed fracture of supraorbital region, rim of orbit, roof of orbit, right.

Associated Injuries. Severe acid burns, left upper extremity and multiple lacerations, abrasions and contusions of body, limbs and face.

Mode of Injury. November 20, 1942, the observation coach in which patient was riding was derailed, rolled down a high embankment and pinned him under the car next to the storage batteries. The supraorbital wound was of penetrating origin. Battery acid ran over the left upper extremity.

Course and Residuals. He was in profound shock when extricated and received blood plasma at the scene of the accident. He was then transported to Brooke General Hospital by ambulance, arriving in moderate shock.

About four hours following injury, his various wounds were debrided and repaired. The orbital wound contained cinders, bits of hay and mud. The foreign material and displaced bone fragments of the frontal sinus, roof and rim of orbit were removed. The orbital fascia had a rather extensive laceration from which protruded periorbital fat. This was amputated in the debridement because it had many foreign bodies in it. The orbital fascia was then closed. The operative tract was irrigated and frosted with sulfanilamide before closure. On January 1, 1943, a small superficial tract of granulation tissue in the upper eyelid was curetted and closed with tantalum wire, healing without delay.

Operation. On April 15, 1943, a coronal incision was made and the scalp flap reflected forward to expose the orbital fascia on the right. A mortise was created about the bone defect in the right supraorbital region. A segment of tantalum metal was cut in such a manner that it would fill the defect in the supraorbital region, repair the defect in the roof of orbit and replace the missing medial two-thirds of the superior orbital rim. The posterior extension formed an angle of approximately 100 degrees with the supraorbital extension. The supraorbital portion was made convex on its anterior surface. Where it joined the posterior extension and replaced the orbital rim it was concave on its inferior aspect. The posterior extension was rather sharply concave to conform to the normal curvature of the roof of the orbit.

Since there was enophthalmos from the defect in the roof of the orbit and laceration of the orbital fascia with escape of some of the orbital fat, the posterior extension was purposely made to exert more pressure, from above, than the normal contour of roof of orbit would exert. This reduced, but did not eliminate, all enophthalmos.

When the tantalum replacement was placed into the prepared bed it locked itself into position into the roof of the orbit and the supraorbital defect so that no anchoring device was thought necessary. Anatomical closure resulted in primary healing.

Postoperative Course. This patient had congenital diplopia on extreme lateral gaze. Following his accident, there was enophthalmos and increased diplopia. The plastic operation reduced his enophthalmos and diplopia but left much to be desired. Therefore, the Ophthalmol-

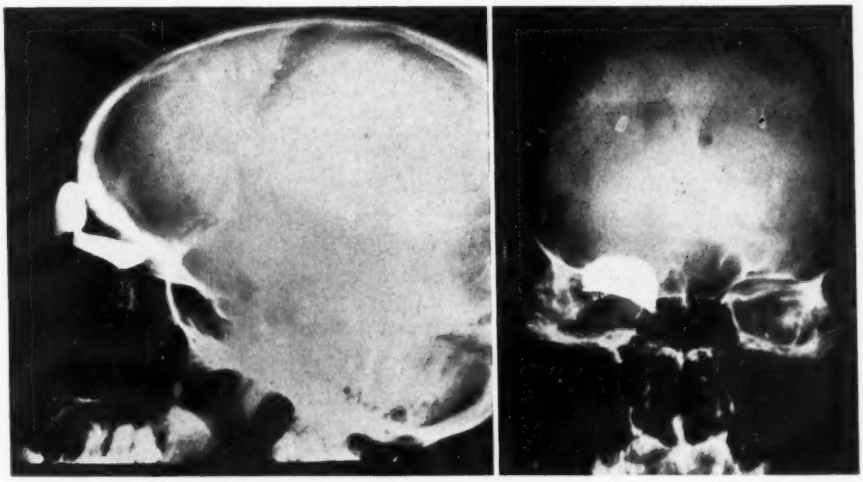


FIG. 5 (*left*). Case 10. Lateral skull film showing replacement of defect in frontal region, frontal sinus, rim and roof of orbit. This demonstrates how tantalum, because of its ductility, can be "adapted to the situation."

FIG. 6 (*right*). Case 10. Posterior-anterior view of tantalum cranioplasty of frontal bone, frontal sinus, rim and roof of orbit. Small opacities are tantalum wire sutures used to close a sinus which was curetted a few weeks prior to cranioplasty.

ogy Department suggested a fascial transplant to correct the enophthalmos. Within 24 hours following the latter procedure a panophthalmitis developed and necessitated removal of the right eye.

Following all operative procedures, with the exception of the last one, done on the Eye Service, convalescence was uneventful.

Case 13. S.B., Brooke General Hospital.

Skull Pathology. Compound, comminuted fracture, right fronto-temporo-sphenoidal and zygoma.

Associated Injuries. (1) Severe laceration, scalp, right fronto-temporo-zygomatic region. (2) Severe laceration, right frontal lobe, postero-lateral. (3) Extensive wound of lateral and posterior aspects, right upper extremity. (4) Compound fracture, lateral epicondyle, right humerus.

Mode of Injury. At a foreign station April 12, 1943, soldier was struck on the head and right arm by a propeller revolving at about 1800 r.p.m. He recalls nothing of the accident or circumstances preceding it. The propeller tips traversed the frontal lobe, cutting a vertical path through the cranium from the midline through the squamous temporal and zygoma. He was treated for shock and the wounds debrided. Sulfonamide medication locally and systemically was instituted. Conservative local treatment was given the wounds.

Course and Residuals. His highest temperature was 102°F. and became normal on the fifth day. Lucid periods began on the third day and gradually increased in length. In spite of this he was somewhat confused and repeatedly removed his head dressings although he was restrained. A continuous cerebrospinal fluid leak was present from the cranial wound and on the eighth day was particularly profuse. He was transferred, by air, to Brooke General Hospital on the twelfth day, April 24, 1943.

The granulating wound in the scalp appeared to be chiefly cerebral herniation, about 2.5 cm. in width, extending from the midline to below the right zygoma on a plane just anterior to the ear. The upper two-thirds was pulsating and cerebrospinal fluid was escaping synchronously with the pulse. On conservative therapy the cerebrospinal fluid leak healed spontaneously, and the granulating surface contracted in width until operation. His mental status had gradually improved to the point that relatives believed him almost normal.

Operation. On June 30, 1943 the scar on the scalp and face was resected down to cranium and the upper end of the resulting scalp wound continued in the coronal plane to the opposite

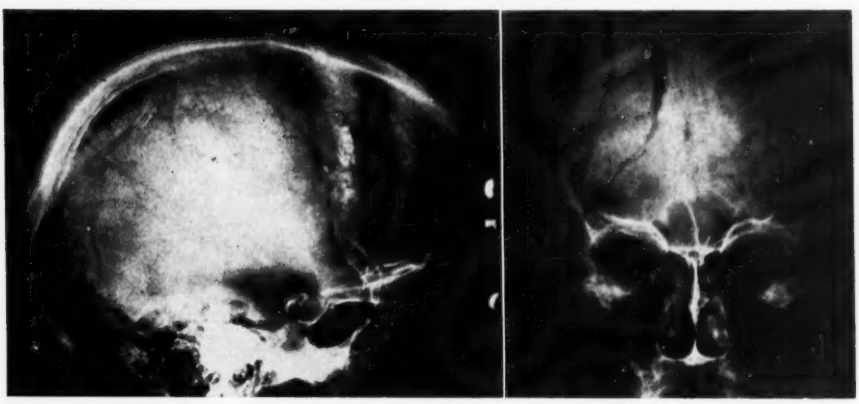


FIG. 7 (*left*). Case 13. Lateral X-ray film demonstrating path of propeller tips through right frontal region.

FIG. 8 (*right*). Case 13. Anterior-posterior skull film showing extent of loose bone fragment which was removed and replaced with tantalum.

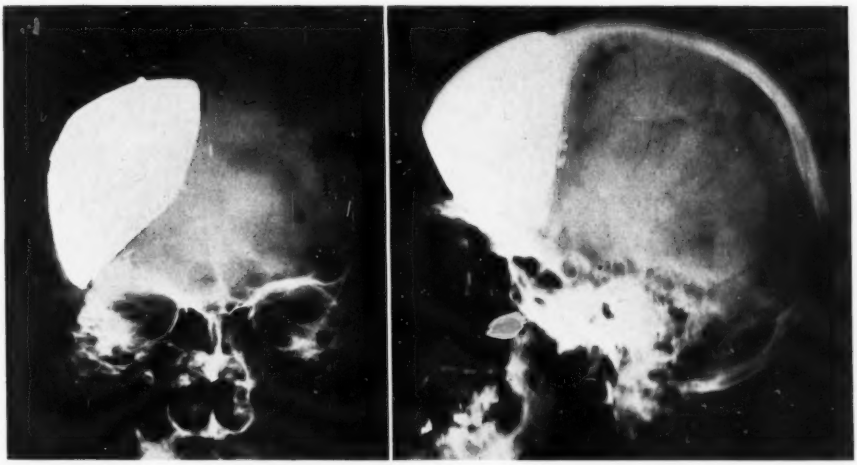


FIG. 9 (*left*). Case 13. Posterior-anterior skull film showing tantalum replacement. Three "glazier points" used to fix the plate can be identified.

FIG. 10 (*right*). Case 13. Lateral skull film following one-stage cranioplasty. Tantalum hemostatic clips indicate level of amputation of right frontal lobe.

zygoma. The scalp was reflected forward almost to the level of the supraorbital ridge. Periosteum was reflected from the loose frontal bone fragment, which was then removed. The dura was defective posteriorly where the propeller passed through it. The dura was turned forward as a flap. In the line of the initial injury the soft granulating cerebral tissue was resected *en bloc*. The underlying white matter was yellowish and contained innumerable cysts of various size. The right frontal cerebral lobe was amputated so far back as the pathological changes extended. This section was carried through the anterior horn of the ventricle to within 1.5 cm. of the interventricular foramen. The right half of the genu of the corpus callosum was incidentally removed. Inferiorly the section was just anterior to the sphenoid ridge. Closure of the dura required reflecting the outer layer, inverting it as a flap, to correct the dural defect. The bone removed from the right frontal region did not fill the cranial defect because the posterior edge had been destroyed in part by the propeller tips. Therefore, the edge of the defect was mortised, and a piece of tantalum was molded by beating, trimmed to size, and then placed in the defect. Small trimmings of tantalum sheet were cut into triangles simulating glazier's points. These were driven into the diploic space about the periphery of the tantalum plate. This accomplished firm fixation of the plate. Closure of scalp was in anatomical layers.

Postoperative Course. Repeated aspirations were required to remove blood-stained cerebrospinal fluid beneath the galea for about two weeks. Several lumbar punctures were also done. His behavior, postoperatively, was characterized by recurrence of some of his post-traumatic aberrations but these gradually subsided over a period of two weeks when his family stated he appeared and behaved the same as before entering the Army.

A thorough psychiatric inventory by Major Martin L. Towler was reported negative. An electroencephalogram on July 26, 1943, was reported to show no indication of disturbance of cortical activity either localized or generalized.

TYPES OF CASES

Fourteen of the twenty-six cases were simple or compound depressed fractures of the skull. Routine treatment of acute cranial trauma was followed by immediate repair of the skull defect. However, some of the patients

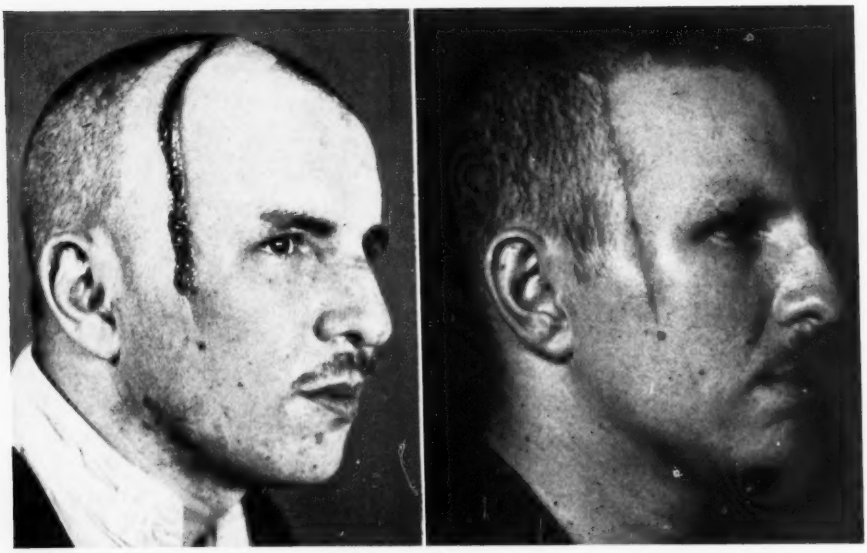


FIG. 11 (*left*). Case 13. Showing granulating wound surface approximately 5 weeks after injury. Exposed cortex was well covered and cerebrospinal fluid leak was healed.

FIG. 12 (*right*). Case 13. Postoperative, showing residual scar. Zygomatic arch may later be restored.

had initial care at other Army hospitals. In these cases, indication for operation was the presence of a cranial defect that gave rise to a feeling of insecurity in the patient or was objectionable from a cosmetic point of view. Continued localizing symptoms, post-traumatic syndrome, or corticomeningeal cicatrix with depressed fracture were considered indications for operation.

TYPE OF OPERATION

Single-stage operations were done in all but two cases. A two-stage procedure would have been wiser in another instance since there was a grossly contaminated wound and the condition of the patient at the time of operation was such as to make haste imperative.

TANTALUM IN SOILED FIELDS

In five cases there was compounding of the fracture with destruction of brain and exposure of brain to the atmosphere for periods longer than thirty hours. Yet these patients were operated upon and tantalum cranioplasty was done following debridement and sulfonamide therapy without later difficulty. We believe that in soiled or infected fields sulfonamides and penicillin make early surgery possible,whereas before these drugs were available, it entailed too great a risk. Also tantalum is well tolerated by tissues. Soiled intracranial wounds, containing various amounts of foreign bodies (hair, straw, cinders, dirt, stones, etc.) occurred in five cases. In one case an

osteomyelitic area of bone was removed four months before cranioplasty. Only three and a half weeks intervened between removal of a brain abscess and tantalum cranioplasty.

Compounding into the frontal sinuses occurred in three instances. In these cases the mucous membranes were removed, the communication with the nose was occluded with muscle stamp, and the bone defect was repaired without complication. Also in three cases the superior rim and roof of the orbit were defective, requiring repair. Restoration of contour and support was readily accomplished due to the ease with which tantalum sheet metal can be worked when cold. The orbital fascia in two of these cases was lacerated and required suture.

ASSOCIATED INJURIES

It should be noted that many patients in this series had associated, moderate to severe, injuries. These ranged from simple fracture to compound, comminuted fractures of the lower extremities and pelvis to severe and extensive lacerations and acid burns.

CRANIECTOMY-CRANIOPLASTY

In one case in the series an intracranial exploration was made through a small opening (previous trephine opening which was enlarged) and the bone was not replaced. Rather, a tantalum replacement was done. Another repair followed removal of a solitary granulomatous lesion of the skull.

Two patients had repair of a cranial defect in the subtemporal region which was made for approach to the gasserian ganglion in a posterior root section for trigeminal neuralgia. One patient had had a subtemporal decompression a year previously for hypertensive meningeal hydrops. Operation was done to save his vision (5 diopters of papilledema, secondary retinal changes, etc.). The residual bulging decompression was disqualifying for full military duty. Because the need for decompression no longer existed the cerebral hernia was reduced at operation and a tantalum plate was fixed in position.

POSTOPERATIVE COMPLICATIONS AND SEQUELLAE

Postoperative complications have been few and none were ascribable to the presence of tantalum. One patient who had a severe, soiled, compound skull fracture containing much foreign material, a few days after operation developed impetigo contagioso on the arms and scalp. Within forty-eight hours thereafter the anterior limb of the operative scar ruptured because of tension created by collected cerebrospinal fluid beneath the scalp flap. This was closed by flamed adhesive strips and an iodine-soaked cotton dental roll over the opening, and healed so that no fluid escaped thereafter. In spite of the impetigo, no infection was discovered beneath the flap in the cerebrospinal fluid collection in specimens aspirated before and following the establishment of open cerebrospinal fluid leak.

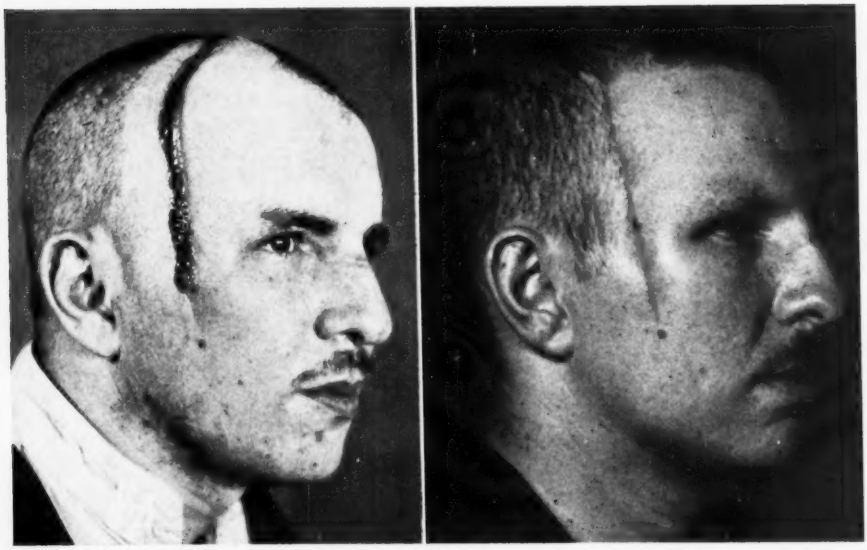


FIG. 11 (*left*). Case 13. Showing granulating wound surface approximately 5 weeks after injury. Exposed cortex was well covered and cerebrospinal fluid leak was healed.

FIG. 12 (*right*). Case 13. Postoperative, showing residual scar. Zygomatic arch may later be restored.

had initial care at other Army hospitals. In these cases, indication for operation was the presence of a cranial defect that gave rise to a feeling of insecurity in the patient or was objectionable from a cosmetic point of view. Continued localizing symptoms, post-traumatic syndrome, or corticomeningeal cicatrix with depressed fracture were considered indications for operation.

TYPE OF OPERATION

Single-stage operations were done in all but two cases. A two-stage procedure would have been wiser in another instance since there was a grossly contaminated wound and the condition of the patient at the time of operation was such as to make haste imperative.

TANTALUM IN SOILED FIELDS

In five cases there was compounding of the fracture with destruction of brain and exposure of brain to the atmosphere for periods longer than thirty hours. Yet these patients were operated upon and tantalum cranioplasty was done following debridement and sulfonamide therapy without later difficulty. We believe that in soiled or infected fields sulfonamides and penicillin make early surgery possible,whereas before these drugs were available, it entailed too great a risk. Also tantalum is well tolerated by tissues. Soiled intracranial wounds, containing various amounts of foreign bodies (hair, straw, cinders, dirt, stones, etc.) occurred in five cases. In one case an

osteomyelitic area of bone was removed four months before cranioplasty. Only three and a half weeks intervened between removal of a brain abscess and tantalum cranioplasty.

Compounding into the frontal sinuses occurred in three instances. In these cases the mucous membranes were removed, the communication with the nose was occluded with muscle stamp, and the bone defect was repaired without complication. Also in three cases the superior rim and roof of the orbit were defective, requiring repair. Restoration of contour and support was readily accomplished due to the ease with which tantalum sheet metal can be worked when cold. The orbital fascia in two of these cases was lacerated and required suture.

ASSOCIATED INJURIES

It should be noted that many patients in this series had associated, moderate to severe, injuries. These ranged from simple fracture to compound, comminuted fractures of the lower extremities and pelvis to severe and extensive lacerations and acid burns.

CRANIECTOMY-CRANIOPLASTY

In one case in the series an intracranial exploration was made through a small opening (previous trephine opening which was enlarged) and the bone was not replaced. Rather, a tantalum replacement was done. Another repair followed removal of a solitary granulomatous lesion of the skull.

Two patients had repair of a cranial defect in the subtemporal region which was made for approach to the gasserian ganglion in a posterior root section for trigeminal neuralgia. One patient had had a subtemporal decompression a year previously for hypertensive meningeal hydrops. Operation was done to save his vision (5 diopters of papilledema, secondary retinal changes, etc.). The residual bulging decompression was disqualifying for full military duty. Because the need for decompression no longer existed the cerebral hernia was reduced at operation and a tantalum plate was fixed in position.

POSTOPERATIVE COMPLICATIONS AND SEQUELLAE

Postoperative complications have been few and none were ascribable to the presence of tantalum. One patient who had a severe, soiled, compound skull fracture containing much foreign material, a few days after operation developed impetigo contagioso on the arms and scalp. Within forty-eight hours thereafter the anterior limb of the operative scar ruptured because of tension created by collected cerebrospinal fluid beneath the scalp flap. This was closed by flamed adhesive strips and an iodine-soaked cotton dental roll over the opening, and healed so that no fluid escaped thereafter. In spite of the impetigo, no infection was discovered beneath the flap in the cerebrospinal fluid collection in specimens aspirated before and following the establishment of open cerebrospinal fluid leak.

OBSERVED REACTION OF TISSUE TO TANTALUM

In one instance revision of a wound was necessary five days postoperative due to slight displacement of the plate. Evidence at the second operation pointed to the formation of a thin, filmy, translucent, gelatinous membrane enveloping the tantalum which must have formed so early as forty-eight hours after the primary operation. Similar observations have been noted when tantalum foil or sheet metal have been examined after being in tissues or between membranes, particularly during secondary craniotomies and peripheral nerve operations. On all occasions, the envelope has been complete and loosely adherent to surrounding tissues. Microscopic examination of the thin envelope has shown it to be composed of "tangled masses of fibrin strands."

CONCLUSIONS

Tantalum metal has been found very useful in neurosurgery. It approaches the theoretical ideal plastic material for replacing lost portions of the cranium.

The nature of the minimal reaction of tissues to the presence of tantalum is advantageous in situations where it has been used. The thin, translucent membrane which forms an envelope about the metal isolates nervous tissues from surrounding tissue thus preventing fixation or traction of subsequently forming scar tissue.

The chief advantages of tantalum from a surgical point of view are its chemical and electrical inertia and ductility.

The work on plastics for repair of cranial defects may well advance cranioplasty and modify our views regarding metallic substances.

The author is obligated to several members of the Surgical Service of Brooke General Hospital for their interest and assistance in the work represented in this communication. Colonel John C. Burch, Chief of Surgery, discovered tantalum for surgery. His advice has been invaluable. Major Otis English, Captain H. L. Reed, former members of the Neurosurgical Section, and Captain W. G. Peacher have done much to make the surgery easier and the presentation more concise.

REFERENCES

1. Burch, J. C. Personal communication.
2. Burke, G. L. The corrosion of metals in tissues; and an introduction to tantalum. *Canad. med. Ass. J.*, 1940, *43:* 125–128.
3. Carney, H. M. An experimental study with tantalum. *Proc. Soc. exp. Biol., N. Y.*, 1942, *51:* 147–148.
4. Fulcher, O. H. Tantalum as metallic implant to repair cranial defects. A preliminary report. *J. Amer. med. Ass.*, 1943, *121:* 931–933.
5. McCall, I. R. Unpublished data, 1943.
6. Pudenz, R. H. The use of tantalum clips for hemostasis in neurosurgery. *Surgery*, 1942, *12:* 791–797.
7. Pudenz, R. H., and Odom, G. L. Meningocerebral adhesions. An experimental study of the effect of human amniotic membrane, amnioplastin, beef allantoic membrane, Cargile membrane, tantalum foil and polyvinyl alcohol films. *Surgery*, 1942, *12:* 318–344.
8. Venable, C. S., Stuck, W. G., and Beach, A. The effects on bone of the presence of metals; based upon electrolysis. An experimental study. *Ann. Surg.*, 1937, *105:* 917–938.

SWIVEL CONNECTION FOR BRAIN SUCTION TIP TO RELIEVE TORSION STRAIN OF RUBBER TUBING

HENRY C. DAHLEEN, M.D.*

Section on Neurosurgery, The Mayo Clinic, Rochester, Minnesota

(Received for publication April 15, 1944)

THE TORSION STRAIN of the stiff rubber tubing which is connected to a curved metal sucker plagues the surgeon whenever he attempts to change the position of the instrument. In order to facilitate the rotation of the sucker tip without rotating the rubber tubing a swivel joint was designed which is interposed between the sucker tip and the rubber tubing. The need for this device was called to the attention of the writer while assistant to Dr. Adson, and its efficacy and common use in the neurosurgical clinic justify its description.

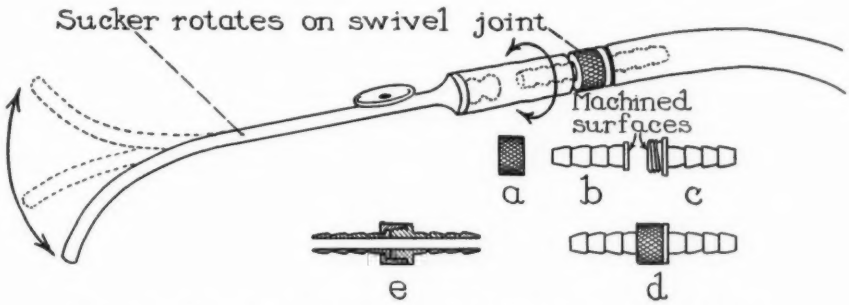


FIG. 1. Swivel device for suction apparatus; *a*, *b*, *c*, *d* and *e* are explained in the text.

The swivel is demonstrated in Fig. 1 as a whole (*d*) and in longitudinal section (*e*) and each of its three parts is shown in the portions of the figure labeled *a*, *b*, and *c*. The outside diameter of the whole device is just that of the suction tubing used. In the assembled unit shown at the top of the illustration, the reader can make out easily the simplicity of the whole unit as it is set up. Note, first, that the rubber coupling hose connecting the sucker tip and the swivel joint is as short as possible, and second, that this rubber coupling is not slipped onto the swivel right up to the hub but instead a small space is left between it and the hub so that part *b* of the device will be free to rotate.

Also notice that there is a flange at the base of the threaded portion of part *c*. This is provided so that when the cap (part *a*) is screwed down to it, a stop will be effected which will prevent the cap from binding the movable part *b*. The joint can be taken apart easily for cleaning when necessary. Lubrication is not needed. Stainless steel or plated brass is used for its manufacture. In actual use, it has been found that there is no leak at the joint. This is possible because of the machined and honed opposing surfaces of parts *b* and *c*, and these surfaces are approximated more closely by any tendency to leak. This not only provides an

* Fellow in Surgery, Mayo Foundation, Rochester, Minnesota.

essentially airtight joint but also gives an almost uninterrupted lumen to the device. Thus there is little chance for blood or other material to clog and dirty the joint.

This unit has been suggested as a separate device rather than as an integral part of the suction tip because it is felt that in this way the swivel can be attached to any piece of suction apparatus and also the cost will be far less than if the joint were an integral part of the suction tip.* This swivel will facilitate the use of any suction device, will prevent the kinking and unruly behavior of the stiff rubber suction tubing and will be found especially useful in neurosurgery, plastic surgery, and ear, nose and throat work.

* At present the instrument cannot be purchased from any manufacturer, but the swivel connection could be made by one's local machinist.

AN EXPERIMENTAL STUDY ON THE USE OF TANTALUM IN THE SUB-DURAL SPACE

CAPTAIN NORMAN C. DELARUE, R.C.A.M.C., ERIC A. LINELL, M.D., AND KENNETH G. McKENZIE, M.D.

Neurosurgical Division, Department of Surgery, and Department of Neuropathology, University of Toronto, Toronto, Ontario

(Received for publication April 17, 1944)

In 1942, Cone, Pudenz and Odom[1] published an experimental study on the use of resorbable animal membranes such as amnioplastin, allantoic and Cargile membranes, as well as tantalum, as a means of preventing meningo-cerebral adhesions. They state: "On the basis of these findings none of the materials studied is considered as ideal for the prevention of meningo-cerebral adhesions. However, until a better material is described, we would recommend tantalum for this purpose."

Because of this statement we have used tantalum in dogs to see for ourselves if one was justified in using it in man to prevent meningo-cerebral adhesions.

METHOD

Under general anaesthesia 12 dogs were operated upon with the same care and operating room facilities utilized on patients. We feel that the results obtained in these dogs would be comparable to the results that we would obtain on a patient.*

Tantalum foil was placed in the sub-dural space over a traumatized area of cerebral cortex. The animals were sacrificed at periods varying from 16 days to 4½ months after the operation.

Using 4 burr holes a large quadrilateral plate of bone was elevated, exposing, symmetrically, the dura mater covering the vertices of both cerebral hemispheres. The dura was incised at 2 to 4 widely separated points and the underlying cortical tissue was traumatized to an approximate depth of 5 mm. At first two areas of cortex were damaged in each hemisphere but, as it was noted that these animals rapidly developed epileptic seizures, only 2 traumata, one in each hemisphere, were inflicted on the later animals of the series. The usual plan of dealing with these symmetrically placed and approximately equal cortical injuries was to suture the dura over the damaged cortex on one side, whereas on the other, a square of tantalum was placed in the sub-dural space over the traumatized cortical area and the dura mater was sutured over it. The bone flap was then replaced and firmly anchored in position.

Apart from the fact mentioned above that a few of the earlier experimental animals with multiple cortical traumata died in a few weeks with severe epileptic seizures, the post-operative course of these dogs was uneventful.

RESULTS

In all these animals there was marked reactive thickening of the dura mater overlying the tantalum. This was beginning to be evident in an animal that died only 16 days after operation. Fig. 1 shows dura mater 4 mm. thick overlying tantalum foil placed in the sub-dural space over the animal's right

* The operations were carried out by Captain Delarue while Resident on Doctor McKenzie's service. The assessment of the results was made by Professor Linell and Doctor McKenzie after Captain Delarue's departure overseas.

FIG. 1. Dura mater thickened to 4 mm. overlying tantalum foil placed in the sub-dural space over this dog's right cerebral hemisphere 2 months before death. The thickened dura mater has compressed the underlying cerebral cortex. The left hemisphere shows the uniform picture of adhesion of dura mater and leptomeninges to a cortical trauma, when tantalum was not placed in the sub-dural space.

hemisphere 2 months before death. It will be noted that the thickened membrane has caused definite downward compression of the underlying cerebral cortex. The dura mater covering this animal's left hemisphere, where no tantalum was interposed, is firmly adherent to the area of cortical trauma but the membrane is not significantly thickened when compared with the reaction caused by the tantalum. As would be expected adhesion of the dura mater to the traumatized leptomeninges and cortex was a uniform finding when tantalum was not placed in the sub-dural space.

In 7 dogs the tantalum was found to be lying free in the sub-dural space when the animal was sacrificed. The best result was in one of these 7 which was killed $3\frac{1}{2}$ months after operation and is shown in Figs. 2 and 3. Fig. 2 shows the free tantalum in position over the left parietal lobe. The dura

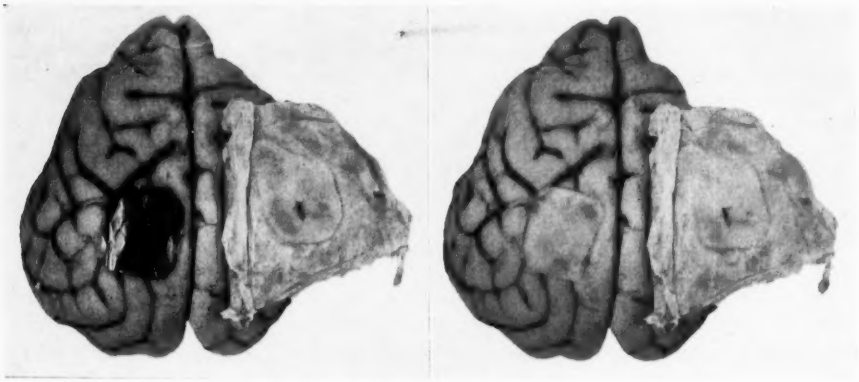


FIG. 2 (*left*). Free sub-dural tantalum over the left parietal lobe of a dog killed $3\frac{1}{2}$ months after operation. The area of dura mater overlying the tantalum is thickened.

FIG. 3 (*right*). Same as Fig. 2, with free tantalum removed, to show thickening of arachnoid membrane underlying the metal.

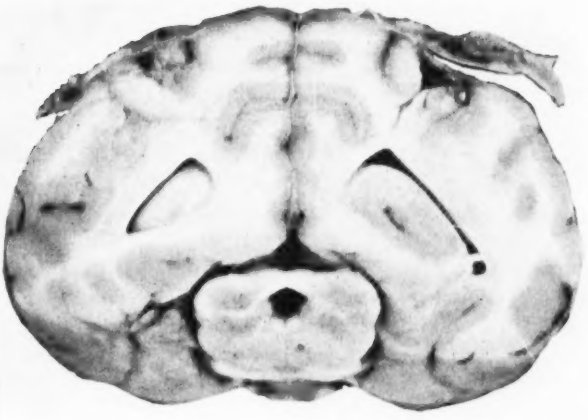


FIG. 4. Partial encapsulation of sub-dural tantalum placed over this animal's right cerebral hemisphere $4\frac{1}{2}$ months before death. The dura mater is adherent to the thickened leptomeninges at the inner margin of the tantalum plate, which has been removed.

mater covering the tantalum has been turned to the right and is thickened over the area that covered the metal. On removal of the tantalum (Fig. 3) the arachnoid underlying the foil shows reactive fibrous thickening. In the other 6 animals in which the tantalum was lying completely free in the sub-dural space the intervals between operation and post-mortem examination were only 16 days, 3 weeks, 1 month, $4\frac{1}{2}$ weeks, $5\frac{1}{2}$ weeks and 2 months (Fig. 1) respectively.

In two additional dogs of the series early encapsulation of the metallic plate by proliferation of fibrous tissue from the thickened dura mater occurred. These animals were sacrificed $3\frac{1}{2}$ and $4\frac{1}{2}$ months after operation and

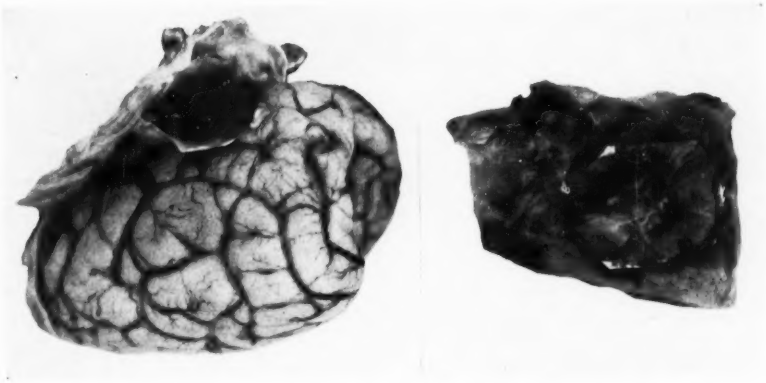


FIG. 5 (*left*). Complete encapsulation of sub-dural tantalum $3\frac{1}{2}$ months after its insertion. The outer wall of the capsule has been removed to show the metal, viewed on edge. The outer wall of the capsule is thickened dura mater. Its inner wall is firmly adherent to traumatized leptomeninges and cerebral cortex.

FIG. 6 (*right*). A second specimen of complete encapsulation of sub-dural tantalum plate, $3\frac{1}{2}$ months after its insertion, viewed from under surface of dura mater. Fragments of adherent cerebral cortex are seen attached to the center of the inner wall of the tantalum capsule.

the brain of the latter animal is shown in Fig. 4. The dura covering the right hemisphere in this case had proliferated at the inner margin of the tantalum to become adherent to the underlying thickened leptomeninges. The metal could be easily removed from its partially formed capsule in both of these animals.

In three dogs, all of which were killed $3\frac{1}{2}$ months after operation, there was complete encapsulation of the tantalum by fibrous tissue which had grown round the under surface of the metal and had become firmly adherent to the leptomeninges and traumatized cerebral cortex. Fig. 5 shows the appearance of the capsule in these animals. It has been opened from its outer side to reveal the contained tantalum which is viewed on edge. The outer wall of the capsule is thickened dura mater. Its inner wall is firmly adherent to the traumatized leptomeninges and cortex. Fig. 6 is of a second of these dogs. It shows completely encapsuled tantalum attached to the under surface of the dura mater. In removing this specimen fragments of adherent cerebral cortex tore away with the inner layer of the tantalum capsule and are seen attached to the center of the latter.

SUMMARY

The gross pathological findings in these 12 dogs can be summarized as follows (E.A.L.):

(1) In 7 animals the tantalum was found lying free in the sub-dural space at post mortem. In one the metal had been in position for $3\frac{1}{2}$ months but in the other 6 the maximum interval between operation and post mortem was 2 months.

(2) In 2 animals killed at $3\frac{1}{2}$ and $4\frac{1}{2}$ months there was early encapsulation of the tantalum.

(3) The remaining 3 animals showed complete encapsulation of the metal with firm adhesion to the underlying cerebral cortex, $3\frac{1}{2}$ months after its insertion into the sub-dural space.

(4) Serious reactive thickening of the dura mater over the tantalum was found uniformly in all 12 dogs, and in many a similar, but slighter, reactive thickening of the underlying arachnoid membrane was present.

CONCLUSION

It is the conclusion of one of us (K. G. McK.) that serious thickening of dura and arachnoid would occur if tantalum foil was placed between dura and underlying traumatized cortex in patients. Furthermore in a certain number the tantalum will become encapsuled with the inner layer of the capsule firmly adherent to the underlying cortical scar. In our opinion the use of tantalum foil between dura and underlying traumatized cortex is contra-indicated.

REFERENCE

1. Cone, W. V., Pudenz, R. H., and Odom, G. L. An experimental study of the prevention of meningocerebral adhesions. *Trans. Amer. neurol. Ass.*, 1942, 117–121.

DARK ADAPTATION, NEGATIVE AFTER IMAGES, TACHISTOSCOPIC EXAMINATIONS AND REACTION TIME IN HEAD INJURIES*

JURGEN RUESCH, M.D.

Division of Psychiatry, University of California Medical School, San Francisco, California

(Received for publication April 20, 1944)

THE DETECTION of diffuse and minor brain damage remains one of the major diagnostic problems in neurology and psychiatry. The lack of appropriate indices of impaired cerebral functioning was especially noticeable in the study of patients suffering from head injuries. The majority of late post-traumatic conditions are characterized by a scarcity of neurological signs and the clinical picture is, in addition, often complicated by psychogenic superstructure. In the search for objective methods which would substantiate the presence of brain damage in these cases, attention was called to a number of visual functions which were shown to be sensitive indicators of changes in brain physiology.[23] In view of these reports it seemed of interest to inquire into the value of visual functions as indicators of structural brain damage. Thus dark adaptation, onset of negative after images, apperception and comprehension following tachistoscopic exposure and reaction time were investigated in 57 patients with head injuries.

The diagnostic value of gross alterations of the visual fields following craniocerebral injuries is well established.[14] The influence of psychological factors in the testing of visual fields is stressed by Gelb and Goldstein.[4] These authors attribute the occurrence of ring scotomata and concentric restricted fields to fatigue following brain injury. Halstead[8] reported on the dynamic visual field, that is, that portion of the peripheral retinal field that can be made to yield the threshold visual impression at the same instant that a form discrimination is being made in the region of the fovea. He found that campimetric and dynamic fields coincide in lesions of the occipital or parietal lobes, but that in frontal lesions the dynamic fields are restricted when compared to the campimetric fields. Investigation of the fields was not confined to examination with white and colored test objects only. Phillips[12] called attention to the use of the flicker phenomenon in neurological diagnostic and Riddell[15] demonstrated its value for the estimation of the density of scotomata. Werner and Thuma[25] applied the same method in the investigation of two groups of mentally deficient children. The critical flicker frequency was lower for the brain injured group at each brightness

* The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of California Medical School. This study is part of an investigation of the sequelae of head injuries being conducted at the Langley Porter Clinic, San Francisco.

level than it was for another group of mentally deficient children without signs of brain injury.

Another group of studies was concerned with deficient perception of motion and with apperception after tachistoscopic exposures. Werner and Thuma[24] showed that children with brain injuries are defective in perception of apparent motion, though they are able to perceive real motion. Pötzl and Redlich[13] described a case of occipital injury with inability to perceive real or stroboscopic movements. A case of occipital and cerebellar injury in which slow and stroboscopic movements could not be perceived at all was reported by Goldstein and Gelb.[7] Ruesch[16] examined acute head injuries with regard to the phi-phenomenon and apperception after tachistoscopic exposure. He found that only a small percentage of cases showed significant impairment. Goldstein,[6] on the other hand, tends to stress the general value of the tachistoscope in the study of head injuries and Altenburger[1] used the same method for the detection of visual field defects.

A third group of studies dealt with visual functions as indicators of altered brain physiology while the subjects were exposed to gas mixtures of low oxygen content. Evans and McFarland[2] studied the effects of oxygen deprivation on the central visual field. They found that while the central visual acuity remains unaffected, the angioscotoma widens progressively with increasing oxygen deprivation until it obliterates almost the entire field. McFarland and Evans[10] demonstrated increased thresholds of light sensitivity after dark adaptation. McFarland and Halperin[11] showed decrease of foveal visual acuity especially at low illuminations. Gellhorn and Spiesman[5] pointed out that there is a lengthening period for the appearance of negative after images under influence of O_2 lack, CO_2 excess and reduction in CO_2 tension of the blood due to hyperpnea. They conclude that these conditions produce a lowered excitability of fundamental nervous mechanisms involved in vision.

The above-mentioned findings clearly demonstrate that the majority of visual functions are dependent on intact anatomical structure of the brain, normal cerebral circulation, and blood chemistry. However, psychological factors such as "attention" determine to a considerable extent the outcome of visual testing. Goldstein,[6] Halstead,[8] Ruesch[16,17,19], and others have shown that the degree of awareness is lowered in patients suffering from brain disease or injury. Impairment of awareness, however, may also occur in distractable, self-preoccupied, or fatigued persons.[3,21]

In the application of visual tests to head-injured patients, these different etiological factors must be considered. In late post-traumatic syndromes the frequent combination of residual signs of brain injury with personality disorders of the neurotic type made it necessary to correlate visual functions with intelligence and personality tests, and with information concerning the severity of the injury. I.Q. and presence of neurological signs are indices of brain damage, whereas the Minnesota Multiphasic Personality Inventory gives a measure of abnormal personality trends.[18] A visuo-motor reaction

time test was included in order to analyze the role of the "speed" factor involved. The selection of the visual tests was based on the commonly accepted theory that dark adaptation, negative after images, and tachistoscopic apperception involve different structures and integration levels of the central nervous system. Thus measurement of the light threshold after dark adaptation represents a simple process of perception. Examination of negative after images involves already higher cerebral functions and tachistoscopic examinations seem to require the greatest amount of "attention."

METHODS

1. *Dark Adaptation:* By means of a bio-photometer manufactured by the Frober Faybor Company in Cleveland, Ohio, and described originally by Jeans, Blanchard and Zentmire, scotopic vision was observed before and after exposure to a bright light.* The observations were made by determining the amount of light necessary for the subject to see 3 of the 5 points of a dice five-spot or quincunx punched out of a metal screen, when the light transmitted through the holes was of decreasing intensity from the left to the right of the quincunx. Six readings were taken: the first one when the subject was unadapted in order to explain the test; the second after 10 seconds in full darkness with eyes closed; the third one between 20 to 30 seconds after termination of a 5-minute bleaching period in which the screen with the five holes had been replaced by a bright light source shining through ground glass. The next 4 readings were taken at $2\frac{1}{2}$-minute intervals each. The results were expressed in millifoot candles referring to the center dot of the quincunx. Since the data showed the greatest scaling of values for the reading after the 5-minute bleach, the results are presented in terms of this single reading only.

2. *Negative After Images:* By means of a Ballopticon, a slide with a picture of a black H on a light field was projected onto a grey-green wall. The size of the projected image was about 25 by 19 cm., the H about 14 by 15 cm. The subject was seated so that the distance from eyes to wall measured 1.6 meters. He was instructed to fix a small black spot on the wall marking the center of the image to be projected later. The illumination of the room was dim to assure the formation of negative after images. The slide was exposed for exactly 5 seconds and the subject was instructed to say "now" immediately upon perception of the negative after image (light H on a dark background). The period from the end of the exposure to the first appearance of the image was timed. Before recording the actual measurements, the subjects were trained for a varying period of time until the task was clearly understood. This was determined by the occurrence of similar values on consecutive readings. Following this trial period, additional exposures were taken and the mean value of the lowest five measurements was considered to be the latency period for the onset of negative after images. In a few instances the subjects reported that they never could see a negative after image and these cases were recorded as having a lengthening period of 30 seconds (failure).

3. *Tachistoscope:* A shutter with exposure speeds of 1/2, 1/5, 1/10, 1/25, and 1/50 of one second was attached to a Ballopticon. Slides with 3 digit numbers were projected onto the wall at the same distance and under the same lighting conditions as described for the negative after images. Five different numbers were shown in succession at each of the varying exposure periods, starting at the fastest speed of 1/50 of one second. The test reading was considered to be the shortest exposure at which all 5 slides were recognized correctly.

4. *Reaction Time:* A flash-light bulb was placed at a distance of about 1.6 meters from the subject, under the same lighting conditions as described before. The subject was instructed to press a hand push-button as soon as he perceived the light. Bulb and push-button were connected with a battery which in turn was in circuit with a relay. A pen attached to the relay recorded any opening and closing of the circuit on a moving tape, so that the reaction time

* I am indebted to Miss R. Gilman for the assistance given me in the course of this investigation.

could be measured directly from the tracing obtained. After a few preliminary trials, the mean value of 10 consecutive measurements was considered to be the representative test reading.

5. *Intelligence and Personality Tests:* Just before the patients left the hospital, they were given a shortened form of the Wechsler-Bellevue Adult Intelligence Scale consisting of Vocabulary, Similarities, Block Design, and Digit Symbol test. These four items were selected because of their high correlation with scores obtained with all eleven subtests. The examination time was thus shortened considerably without sacrificing the validity of the procedure. In addition to the intelligence tests, the Minnesota Multiphasic Personality Inventory and a specially prepared Complaint Scale were given to all subjects. The results obtained with these methods have been published separately.[18]

6. *Statistics:* Differences between means were considered significant when the difference divided by the probable error of the difference equalled or exceeded 4.0. Correlations were determined by the product-moment method. Following common use, coefficients ranging from 0 to 4 times the probable error of the coefficient of correlation were considered negligible, from 4 to 6 times as indicating a slight relationship, and above 6 times as expressing a substantial relationship.

CASE MATERIAL

Twenty-five unselected patients with recent head injuries (acute cases) were compared with 32 patients (chronic cases) who suffered from prolonged post-traumatic syndromes. In this latter group the accidents dated back from 6 months to more than 5 years. No diagnostic selection of cases was made except for the fact that the patients had to be cooperative and had to understand the instruction, thus excluding extremely dement and confused subjects. The case material used in this report coincides with the detailed description of head-injured patients given elsewhere.[18] The majority of the patients were males, except for 3 females, in each series. Ages and I.Q. of the patients are given in Table 1. In 15 of the acute and 15 of the chronic cases there were signs of brain damage as evidenced by bloody spinal fluid, inequality of tendon reflexes, presence of pathological reflexes, cranial nerve palsy, convulsions or confusion. In addition to the patients, 25 hospital employees were subjected to the same tests; 17 of these were females, 8 were males. Though these subjects do not constitute a matched control group, the results obtained from this series helped in the evaluation of the data.

TABLE 1

Mean values and standard deviations of test results

Number of Cases	Dark Adaptation		After Image		Tachistoscope		Reaction Time		Intelligence		Age	
	Milli-foot candles		Latency period in seconds		Exposure in hundredths of 1 second		Reaction time in tenths of 1 second		I.Q.		Years	
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
25 Acute Cases	2.8	1.4	13.3	7.8	6.3	5.7	5.4	2.3	99	15	45.3	12.6
32 Chronic Cases	1.7	1.4	7.6	2.8	3.6	5.1	4.5	1.6	110	16	37.3	15.4
25 Controls	—	—	7.1	2.8	2.6	3.1	3.0	0.7	—	—	28.6	8.4

DATA

1. *Difference between Acute and Chronic Cases.* In Table 1 mean values and standard deviations are given for the various test results. The figures for

the acute cases are more abnormal than those for the chronic cases; the controls have the lowest, that is, the most normal values for all three types of cases studied. Between the controls and the acute cases, statistically significant differences exist for all the variables. In the acute cases the onset of negative after images is significantly lengthened as compared with the chronic patients. The difference obtained between acute and chronic cases for tachistoscopic examinations approaches significance: the difference of the means divided by the probable error of the difference ($D/PE_D = 3.0$) indicates that there are 97.9 chances out of 100 that this constitutes a true difference.

TABLE 2

Intercorrelation of test results

	Dark adaptation	After images	Tachisto-scope	Reaction time	Intelli-gence	Age
Dark adaptation		+.23 ±.10	+.08 ±.105	−.03 ±.105	−.11 ±.103	+.53 ±.076
After images	+.57 ±.064		+.42 ±.086	+.36 ±.091	−.27 ±.097	+.32 ±.094
Tachistoscope	−.15 ±.091	−.04 ±.094		+.50 ±.080	−.41 ±.087	+.02 ±.105
Reaction time	+.03 ±.094	+.01 ±.094	+.20 ±.090		−.25 ±.098	+.33 ±.094
Intelligence	.00 ±.094	−.01 ±.094	−.10 ±.092	−.13 ±.092		−.35 ±.092
Age	+.15 ±.091	+.38 ±.081	+.56 ±.065	+.23 ±.084	+ 15 ±.091	

ACUTE CASES (25 patients)

CHRONIC CASES (32 patients)

2. *Association with Age, Intelligence, Personality and Complaints.* In order to analyze whether these differences are an expression of brain injury or of other factors, the results obtained were correlated with age, intelligence, the Minnesota Personality Inventory, and the Complaint Scale. From Table 2 one can see that, in the acute cases, dark adaptation is to a considerable extent a function of age ($r = +.53$). The onset of negative after images is in both the acute ($r = +.32$) and chronic ($r = +.38$) cases to an equal extent influenced by age; intelligence seems to prolong the onset of after images in the acute cases to a minor degree ($r = -.27$). Tachistoscopic results seem to be a function of intelligence in the acute cases ($r = -.41$) and of age in the chronic patients ($r = +.56$). Reaction time in both groups of patients is fairly independent of intelligence ($r = -.25$ and $-.13$) but is to a minor degree a function of age ($r = +.33$ and $+.23$). Correlation of the results with the Minnesota Multiphasic Personality Inventory and the Complaint Scale[18] did not reveal any significant association.

3. *Association with Brain Damage.* In order to analyze the association of the test results with persistent signs of brain damage following the initial loss of consciousness, the method described by Ruesch et al.[18] was used to classify the cases according to the severity of the injury. In addition, the patients were separated according to the presence or absence of neurological signs. Only the results obtained with the negative after images showed a significant separation of patients within the acute group: those with neurological signs had a latency period of 16 seconds, those without, of 8.4 seconds.

4. *Intercorrelation of the Visual Tests.* The intercorrelation of the various tests in the acute cases indicates that tachistoscopic results, negative after images, and reaction time are more closely related to each other ($r = +.36$, $+.42$, $+.50$) than to dark adaptation ($r = -.03$, $+.08$, $+.23$). In the chronic cases there exists a relationship between dark adaptation and negative after images ($r = +.57$).

COMMENT

The interpretation of the differences found between acute and chronic patients is guided by consideration of the results obtained in the control group. Acute head injuries have the most abnormal values, while the figures of the chronic cases tend to approximate those of the control group. The onset of negative after images proves to be the most significant of the tests used. The lengthening period found in the acute cases holds in spite of age. It is associated to a moderate degree ($r = -.27$) with low I.Q., indicating its relationship to intellectual impairment. The delayed onset is, in addition, a function of brain damage, since acute cases with neurological signs show a much greater lengthening than cases without such signs. In the chronic cases no association between latency period and intelligence or severity of the brain damage could be demonstrated.

Tachistoscopic apperception is delayed in the acute group and the difference between acute and chronic cases approaches significance. However, no association between presence of neurological signs and delayed apperception could be demonstrated. In the acute series, tachistoscopic results are related to intelligence ($r = -.41$). This is probably an expression of intellectual impairment since tachistoscopic results in the chronic cases are independent of intelligence, but are rather a function of age, thus restricting the use of this method in late post-traumatic syndromes. The determination of light threshold after dark adaptation and reaction time did not yield significant differences between acute and chronic cases.

An explanation of the lengthening period for the appearance of negative after images may be found in some physiological findings. Lindquist and LeRoy[9] showed that cerebral oxygen consumption and cerebral circulation are decreased in dogs following a head injury. Schnedorf et al.[20] found reduced oxygen consumption in man after head injury, and Stone, Marshall and Nims[22] reported post-traumatic changes in pH and blood chemistry. All these findings point to the fact that metabolic changes are present after

head injury. Since the latency period in negative after images is lengthened by O_2 lack, CO_2 excess and reduced CO_2 tension of the blood (Gellhorn and Spiesman[5]), it is safe to assume that similar factors might have produced the lengthening in our acute cases.

The causes for the prolonged apperception time after tachistoscopic exposure in the acute cases are difficult to determine. That this aspect is not related to personality is shown by the lack of association with number or type of complaints or personality inventories. The absence of any significant association with presence or absence of neurological signs, or severity of the injury, indicates that the tachistoscope measures one aspect of head injury which is not expressed in massive tissue destruction. Nevertheless, the slower apperception of the acute cases must somehow be related to the injury. As mentioned above, age and intelligence are determining factors in tachistoscopic examinations. Both progressing age and decline of intellectual functions are associated with decline of brain weight. Similarly clinical evidence points to the frequent occurrence of cerebral atrophy following head trauma in absence of any neurological signs. Therefore, it is possible that the delayed apperception after tachistoscopic examination may be an expression of minor or diffuse brain damage, a hypothesis which has been repeatedly stipulated by Goldstein.[6] This theory is also corroborated in our data by other findings. It has been established elsewhere[6,16,19] that slowing of mental functions is an outstanding sign of brain damage. The intercorrelations ($+.42$, $+.36$, $+.50$) of tachistoscopic results, negative after images and reaction time, demonstrate the retardation and slowing of mental functions in the acute cases, whereas light threshold after dark adaptation shows much lower intercorrelations with the other tests ($+.23$, $+.08$, $-.03$), probably because the time factor is not involved. With increasing recovery and remoteness from the date of the injury (chronic cases), the slowing recedes as evidenced by the low intercorrelations of the visual tests containing a time factor ($-.04$, $+.01$, $+.20$). It would be a fallacy, however, to attribute the slowing of mental functions to the presence of brain damage only. Disturbances of attention, apprehension and fatigue may influence visual apperception[3,21], and neurotic individuals often complain of such disturbances. One has to consider that the effect of injury is not only a physical one, but that the psychological shock suffered may frequently lead to the development of anxiety, apprehension and other neurotic symptoms. Influence of such psychogenic factors on the outcome of test results should, therefore, not be disregarded.

Another interesting aspect of visual functions in post-traumatic syndromes is revealed by the fact that dark adaptation correlates higher with negative after images than with any of the other tests (acute cases, $r = +.23$; chronic cases, $r = +.57$). This finding can be interpreted by the commonly accepted theory that "retinal" factors are more predominant in these two tests than in tachistoscopic apperception and reaction time in which "attention" and higher cerebral functions are involved.

Of incidental interest is the finding that I.Q. in the acute group declines

with progressing age ($r = -.35$), thus indicating that older individuals suffer a relatively greater intellectual impairment. This fact is corroborated by the clinical findings of slower recovery and greater incidence of confusional states after head injury in older individuals.

The experiences gained in this investigation lead to the conclusion that testing of negative after images and of tachistoscopic apperception are brief and practical procedures. Interpretation of the results obtained with these methods, however, cannot be done without consideration of factors such as age and I.Q. Extreme deviations, therefore, are useful and significant for diagnostic purposes only. For prognostic use, however, repeated tests on the same individuals are of great value. Improvement of performance is definite evidence of previous impairment, and lack of further improvement indicates that a relatively stable post-traumatic level has been attained. Thus it seems that visual examination methods have a definite place in clinical procedures, since they may reveal defects and show improvement where other methods fail.

SUMMARY

1. Light threshold after dark adaptation, latency period for onset of negative after images, apperception after tachistoscopic exposure, and visuomotor reaction time were determined in a series of 25 patients with recent head injuries, in 32 patients suffering from prolonged post-traumatic syndromes, and in 25 control subjects.

2. The influence of age, I.Q., severity of the injury, presence of neurological signs, time elapsed since the injury, and personality features on the outcome of these tests are analyzed and discussed.

3. A lengthening period for the onset of negative after images could be demonstrated for patients with recent head injuries. The acute cases with persistent signs of brain damage had a significantly longer latency period than acute cases without such signs. Apperception after tachistoscopic exposure proved valuable in acute cases but was not associated with the presence of persistent neurological signs. Light threshold after dark adaptation and reaction time did not show significant differences between acute and chronic patients.

REFERENCES

1. Altenburger, H. Die Aufdeckung hemianopischer Gesichtsfelddefekte durch die tachystoskopische Methode. *Arch. Psychiat. Nervenkr.*, 1929, *88:* 477–485.
2. Evans, J. N., and McFarland, R. A. The effects of oxygen deprivation on the central visual field. *Amer. J. Ophthal.*, 1938, *21:* 968–980.
3. Franz, S. I., et al. Studies in cerebral function. I–IX. *Univ. Calif. Publ. Educ. Philosoph. Psychol.*, 1933, *1:* 65–136.
4. Gelb, A., and Goldstein, K. Über Gesichtsfeldbefunde bei abnormer "Ermüdbarkeit" des Auges. [sog. "Ringskotome"] *v. Graefes Arch. Ophthal.*, 1922, *109:* 387–403.
5. Gellhorn, E., and Spiesman, I. G. The influence of hyperpnea and of variations of the O_2- and CO_2-tension in the inspired air upon after-images. *Amer. J. Physiol.*, 1935, *112:* 620–626.
6. Goldstein, K. After effects of brain injuries in war. Their evaluation and treatment. The application of psychologic methods in the clinic. *New York: Grune & Stratton*, 1942, 244 pp.

7. Goldstein, K., and Gelb, A. Zur Psychologie des optischen Wahrnehmungs- und Erkennungsvorganges. *Z. ges. Neurol. Psychiat.*, 1918, *41:* 1–142.
8. Halstead, W. C. Function of the frontal lobe in man: the dynamic visual field. *Arch. Neurol. Psychiat., Chicago,* 1943, *49:* 633.
9. Lindquist, J. L., and LeRoy, G. V. Studies of cerebral oxygen consumption following experimental head injury. *Surg. Gynec. Obstet.*, 1942, *75:* 28–33.
10. McFarland, R. A., and Evans, J. N. Alterations in dark adaptation under reduced oxygen tensions. *Amer. J. Physiol.*, 1939, *127:* 37–50.
11. McFarland, R. A., and Halperin, M. H. The relation between foveal visual acuity and illumination under reduced oxygen tension. *J. gen. Physiol.*, 1940, *23:* 613–630.
12. Phillips, G. Perception of flicker in lesions of the visual pathways. *Brain*, 1933, *56:* 464–478.
13. Pötzl, O., and Redlich, E. Demonstration eines Falles von bilateraler Affektion beider Okzipitallappen. *Wien. klin. Wschr.*, 1911, *24:* 517.
14. Rand, C. W. Alterations in the visual fields following craniocerebral injuries. *Arch. Surg., Chicago,* 1936, *32:* 945–989.
15. Riddell, L. A. The use of the flicker phenomenon in the investigation of the field of vision. *Brit. J. Ophthal.*, 1936, *20:* 385–410.
16. Ruesch, J. Intellectual impairment in head injuries. *Amer. J. Psychiat.*, 1944, *100:* 480–496.
17. Ruesch, J. The diagnostic value of disturbances of consciousness. *Dis. nerv. Syst.*, 1944, *5:* 69–83.
18. Ruesch, J., Harris, R. E., and Bowman, K. M. Pre- and post-traumatic personality in head injuries. *Res. Publ. Ass. nerv. ment. Dis.*, 1944, *24.* (In press)
19. Ruesch, J., and Moore, B. E. Measurement of intellectual functions in the acute stage of head injury. *Arch. Neurol. Psychiat., Chicago,* 1943, *50:* 165–170.
20. Schnedorf, J. G., Munslow, R. A., Crawford, A. S., and McClure, R. D. Anoxia and oxygen therapy in head injury. *Surg. Gynec. Obstet.*, 1940, *70:* 628–631.
21. Simonson, E., and Enzer, W. Measurement of fusion frequency of flicker as a test for fatigue of the central nervous system. *J. Industr. Hyg.*, 1941, *23:* 83–89.
22. Stone, W. E., Marshall, C., and Nims, L. F. Chemical changes in the brain produced by injury and by anoxia. *Amer. J. Physiol.*, 1941, *132:* 770–775.
23. Van Liere, E. J. Anoxia. Its effect on the body. *Chicago, Ill.: University of Chicago Press*, 1942, 269 pp.
24. Werner, H., and Thuma, B. D. A deficiency in the perception of apparent motion in children with brain injury. *Amer. J. Psychol.*, 1942, *55:* 58–67.
25. Werner, H., and Thuma, B. D. Critical flicker-frequency in children with brain injury. *Amer. J. Psychol.*, 1942, *55:* 394–399.

CEREBELLAR MEDULLOBLASTOMA WITH VERIFICATION NINETEEN YEARS AFTER THE ONSET OF SYMPTOMS

FRANC D. INGRAHAM, M.D., AND ORVILLE T. BAILEY, M.D.

Departments of Surgery and Pathology, Harvard Medical School, and Surgical Services of the Peter Bent Brigham and The Children's Hospitals, Boston, Massachusetts

(Received for publication May 1, 1944)

MEDULLOBLASTOMAS are usually considered solid, midline cerebellar tumors of childhood with rapid progression[1] but with excellent, if usually temporary, response to roentgen therapy. Because these characteristics have become so firmly established, it may be of interest to record an instance of cerebellar medulloblastoma which departs clinically in almost all respects from the usual behavior of this tumor but has the typical histological appearance.

REPORT OF CASE

A single, American school girl of 15 was admitted to the Peter Bent Brigham Hospital September 19, 1924. The family history and past history were irrelevant. She had been quite well until 2½ months before entry, when she began to have severe frontal headaches. During the month preceding hospitalization the headaches had become more severe and had been associated with vomiting. Some dizziness accompanied the most severe headaches and in the month before admission she had difficulty in reading fine print. Physical examination at that time showed marked suboccipital tenderness and a definite cracked-pot sound. There was choking of both optic discs (6 diopters), marked reduction of visual acuity, bilateral sixth nerve palsy and incoordination of movement in all extremities.

Operation I. A diagnosis of central cerebellar tumor was made and a suboccipital exploration was carried out by Dr. Percival Bailey. A portion of his operative note follows:

"On opening the dura the surfaces of the hemisphere looked rather vascular and showed no evidence of tumor. There was a rather marked pressure cone. Puncture of the left hemisphere met with slight resistance at a depth of about 5 cm. Puncture of the right hemisphere at a depth of 5 cm. came down upon yellowish fluid mingled with dark blood. About 15 cc. of fluid were removed. Since the cystic tumor was obviously too deep to be removed, the wound was closed carefully in layers as usual. The patient was in good condition at the end of operation."

Course. At the time of discharge 26 days after admission the patient had recovered remarkably. She was able to walk without assistance and the papilledema had almost entirely subsided.

Interval Note. Two years later (1926) a report by letter stated that she was in perfect health and was receiving roentgen therapy. Several treatments were given, the last one at the end of March, 1926. In March, 1927, a single additional treatment was administered. Unfortunately, it has been impossible to determine what dosage was used in these treatments.

Second Admission. She reentered the hospital May 16, 1927, for recurrent headache of 4½ months' duration. During the 18 days preceding admission she had noticed slight unsteadiness of the right hand. Physical examination showed fulness of the suboccipital decompression, slight tenderness in that region, unequal, dilated pupils, hazy optic discs, a diminished right knee jerk and absent left knee jerk. A diagnosis of recurrent right cerebellar cyst was made.

Operation II. Reexploration was carried out by Dr. Harvey Cushing. This was done at the time when there was great interest in the endothermy apparatus, which had only recently been introduced into neurosurgery by Doctor Cushing.[2] In fact, it was on this occasion that

the instrument now in general use was first employed. Doctor Cushing's operative note follows:

"Although the child complained considerably during the earlier stages of this exploration it was possible to get the cerebellum again well reexposed and it was only when she had an attack of vomiting from manipulations in the region of the fourth ventricle that ether was temporarily given.

"There had been a good deal of new bone formation in the defect, which made the reflection of the flap somewhat difficult.The cutting current was used with the new apparatus

FIG. 1. Roentgenogram in 1943, showing destruction of the sella turcica, calcification in the tumor and the old operative defect.

which had just arrived. I finally got down into the posterior cistern in the region of the foramen and found the upper part of the cord and the calamus quite normal in appearance. An abundance of fluid was coming from the ventricle and I did not feel therefore that there could possibly be a cerebellar tumor, which I had anticipated finding. Nevertheless, a median incision was made with the electro-current down fairly well into the uvula, which seemed to me a little prominent. However, I was rather half-hearted about this I fear. A puncture was made into each hemisphere without meeting resistance or getting fluid.

"There was no fulness of either cerebellar hemisphere and I was under the impression that in all probabilities no tumor is present, though, of course, I may be mistaken in this.

"I was held by bleeding in the right lateral angle of the exploration where a number of clips were found and where there must have been a good deal of bleeding at the previous operation.

"The flaps were then replaced and closed in layers, the last stages by Doctor Cairns.

"It should be stated from the diathermia standpoint that the cutting current worked excellently in this case but on one occasion a shock went through to the anesthetist."

Course. The patient made an uneventful recovery from this procedure and was discharged one month after admission.

Interval Note. She reported by letter several times in the next few years and considered herself to be in perfect health except for her left external strabismus. This was corrected by operation in 1934. She was well until October of 1942 when she began to have double vision

FIG. 2. Roentgenogram in 1943. Calcification is seen through the suboccipital defect.

and a tendency to stagger toward the left on walking. Her condition became progressively worse and there was an increasing tendency to drowsiness.

Third Admission. She was readmitted to the hospital May 3, 1943, at which time she showed reduction of visual acuity, secondary optic atrophy, unequal pupils, left facial weakness, and a positive Romberg sign with tendency to fall to the left. There was slurring speech and dysmetria, particularly on the left. Roentgenograms of the skull showed destruction of the sella turcica with complete erosion of the posterior clinoids and an irregular mass of calcification high in the posterior fossa at the midline (Figs. 1 and 2).

Operation III. At exploration, the vermis was divided and tumor was encountered adjacent to the aqueduct at a depth of about 5 cm. A small piece of tumor was removed and circulation of cerebrospinal fluid restored. It was obviously impossible to do a total extirpation.

Course. The patient recovered slowly. During convalescence she was given a course of roentgen therapy to the region of the tumor (cross-fired through two portals, 1500 r each) and discharged July 14, 1943. She was readmitted 9 months later for additional irradiation and at this time she was free from symptoms.

It is noteworthy that during the long interval between the second and third operation the patient was married, did her own housework, and brought up one child.

Pathological Studies. The material removed in 1943 consisted of several fragments of soft, grayish-pink tissue measuring in aggregate approximately 0.5 × 0.4 × 0.4 cm. Paraffin sections

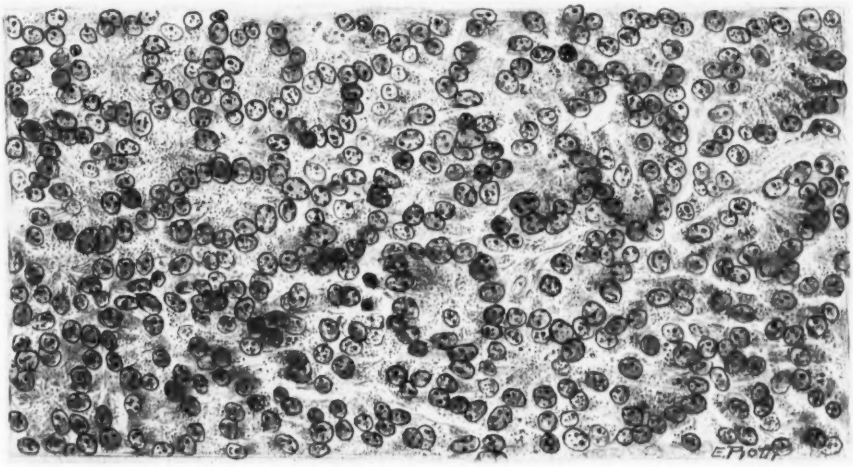


FIG. 3. Camera lucida drawing of tumor obtained in 1943. The cellularity and the rosette formation of the medulloblastoma are shown. Mallory's phosphotungstic acid-hematoxylin stain (×600).

were stained with hematoxylin and eosin, eosin-methylene blue, and Mallory's phosphotungstic acid-hematoxylin, and by the Foot method for reticulum.

There were several fragments of cerebellum which were normal except for areas of recent hemorrhage, presumably operative. Two fragments, however, were from the tumor and showed its histological characteristics well. The neoplasm was composed of closely packed round or oval cells with abundant dispersed chromatin. In a fair number of nuclei prominent nucleoli were seen. Occasional mitotic figures were encountered in most areas but in a few fields they were very numerous. The cytoplasm was scanty and took a pale stain. These cells were usually arranged in uniform sheets but in some areas there was well marked rosette formation (Fig. 3). Within the rosettes and elsewhere among the neoplastic cells, very delicate brownish fibrils were demonstrated with the phosphotungstic acid-hematoxylin technique (Fig. 4). From place to place, astrocytes were found among the cells of the type already described, some of them being fibrous and others protoplasmic. The cells of the tumor were separated into islands by numerous delicate capillaries and accompanying collagenous connective tissue. Stains for reticulum showed this to be confined to the neighborhood of the capillaries. There were no lumina, *blepharoplasten* or other features of ependymoma.

COMMENT

When dealing with brain tumors, as well as with other neoplasms, a definite correlation can usually be made between the clinical findings and

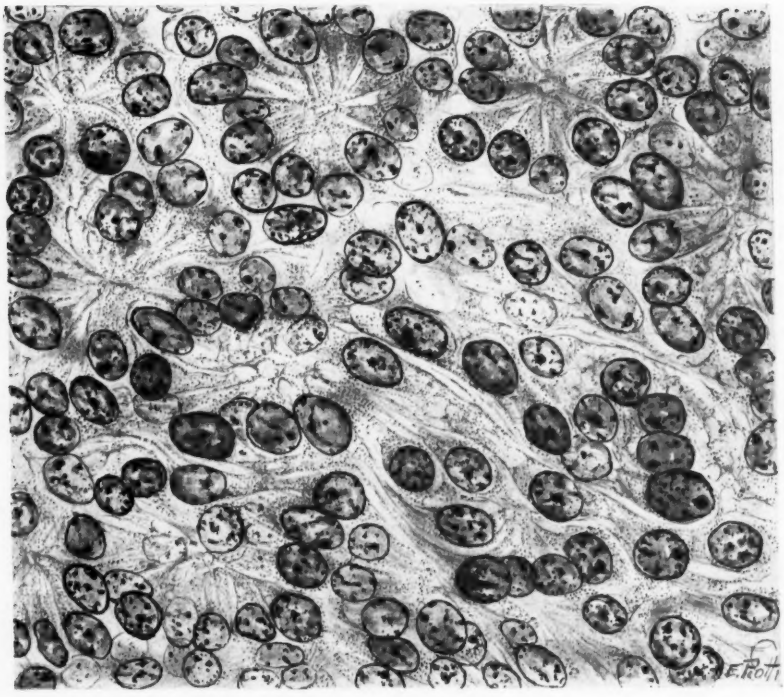


FIG. 4. Camera lucida drawing of medulloblastoma obtained in 1943. Some of the cells contain prominent nucleoli and resemble early neuroblasts. The rosettes contain delicate fibrils and similar fibrils are found among the tumor cells which are not in rosette arrangement. Mallory's phosphotungstic acid-hematoxylin stain (×1300).

the pathological characteristics, but a certain number of instances must be expected in which variations exist. The patient described in this paper presents many complex and bizarre problems in relating the clinical manifestations to the type of tumor finally obtained for histological study.

There can be no doubt of the diagnosis of medulloblastoma on the tissue removed in 1943. The undifferentiated cells, the early and abortive neuroblasts mixed with glia, the rosette formation, and the presence of vascular and collagenous stroma[3] are all characteristic of the medulloblastoma. We have been somewhat doubtful of the current opinion that the tumors now classified as medulloblastomas are actually derived from medulloblasts, that is, from cells capable of differentiation into neuroblastic and glia elements. This question in the classification of brain tumors is largely of academic interest and is not the immediate concern of this report.

Tumors with the histology of this one usually occur in the midline of the cerebellum and progress rapidly to a fatal termination. There were no symptoms in the patient herein discussed until she was 15, rather older than ex-

pected but by no means an impossible age of onset. The first operation demonstrated a cyst of the cerebellum without tissue being obtained for determination of the nature of the tumor. Medulloblastomas only rarely become cystic. Again, the neoplasm under discussion showed extensive calcification. Medulloblastomas of the cerebellum rarely calcify though those of the cerebrum often do. While irradiation was given in 1926 and 1927, the amount was much smaller than the dosage now regarded as adequate to hold a medulloblastoma in check. Yet the patient survived with a useful existence for 19 years after the first operation before symptoms returned for the third time and a fragment of medulloblastoma was at length secured.

In order to correlate the clinical history as presented with the pathological study of the tumor removed in 1943, an hypothesis must be set up to explain the deviations from the usual syndrome of cerebellar medulloblastoma. Several are possible. One might assume that the patient had two tumors, a cystic astrocytoma or hemangioma in 1924 with subsequent development of an independent medulloblastoma. It is also possible to postulate that the original cystic tumor had undergone a great change in histology over a period of years. Again, it is possible that one portion of the tumor was much more malignant than the rest.

We are inclined to favor still another hypothesis—that the tumor was a medulloblastoma in 1924 with an unusually long survival period, perhaps extended by the inadequate roentgen therapy. If so, the tumor must have behaved in a most unusual way for the roentgen therapy was not repeated as it should be to hold a medulloblastoma in check and no radical attack has been made upon the tumor surgically.

Whichever one of these hypotheses is correct, and there seems to be no definitive way of choosing among them, the history of this patient seems significant in illustrating unusual possibilities in the behavior of medulloblastomas of the cerebellum.

SUMMARY

A cystic tumor was demonstrated by aspiration of fluid in the cerebellum of a girl of 15 in 1924. Roentgen therapy, of inadequate dosage, was given in 1926 and 1927. Symptoms recurred in 1927, but improved after a negative exploration. Following another asymptomatic interval, symptoms again appeared in 1943. At that time, a medulloblastoma was demonstrated. This patient thus presents marked deviation from the usual syndrome of cerebellar medulloblastoma.

REFERENCES

1. Bailey, P. and Cushing, H. Medulloblastoma cerebelli. A common type of midcerebellar glioma of childhood. *Arch. Neurol. Psychiat., Chicago*, 1925, *14:* 192–223.
2. Cushing, H. Electro-surgery as an aid to the removal of intracranial tumors. With a preliminary note on a new surgical-current generator by W. T. Bovie, Ph.D., Chicago. *Surg. Gynec. Obstet.*, 1928, *47:* 751–784.
3. Wolbach, S. B. and Bailey, P. The histology of tumors of the cerebrum and cerebellum. *J. Med. Res.*, 1923, *44:* 104–106.

PARALYSIS IN FLEXION AND TREMOR IN THE MONKEY FOLLOWING CORTICAL ABLATIONS*

W. K. WELCH, M.D., AND MARGARET A. KENNARD, M.D.†
Laboratory of Physiology, Yale University School of Medicine, New Haven, Connecticut

(Received for publication May 9, 1944)

INTRODUCTION

PARALYSIS WITH flexion attitude, spasm and contracture in the lower extremities, is well known in injury or disease of the spinal cord. Clinically cerebral lesions inducing flexion paraplegia have been described by Demange,[4] and others [1,6,10,11,12,13,14]. The syndrome occurs with extensive degenerative cerebral disease, most frequently of arteriosclerotic origin. Marie and Foix[11] and Alajouanine[1] have emphasized lesions in the paracentral lobules and subjacent white matter. Verhaart[13] has stressed lesions of the central gyri and frontal lobe, and, in one patient, attributed the flexion pattern to decerebration above the red nucleus.[14] The lesions are often diffuse and Herman's attempt to localize the significant one in his case was impeded by too numerous and extensive arteriosclerotic changes.[6] This subject has been recently reviewed by Daniels.[3] Unilateral flexion paralysis sometimes results from capsular hemorrhage[15] and Holmes and Sargent[8] described flexion spasms of the legs in a number of patients with the sagittal sinus syndrome.

Few experimental observations have been recorded. Alajouanine[1] produced paraplegia in flexion in the dog by bilateral, midline cortical ablations. Hines[7] noted permanent shortening of the hamstring muscles following unilateral ablation of areas 4 and 4*s* in monkeys. Walshe[16] correlated extensor tonus following cord injury with damage to the pyramidal tract, and flexor reflex exaggeration with more extensive lesions involving extrapyramidal tracts as well. Flexion of the extremities, however, is not remarkable following unilateral or bilateral *seriatim* ablations from area 6, the principal extrapyramidal region of the cortex. This paper describes the experimental production of flexion paralysis in monkeys by simultaneous extirpation of area 6 (including its mesial surface) bilaterally.

Tremor, which appeared also in these animals, has been previously noted as occurring in monkeys with bilateral lesions of area 6[9]. The augmentation of the involuntary movements associated with cerebellar destruction[5] and with basal ganglia lesions[9] by additional removal of area 6 has been discussed.

MATERIALS AND METHODS

Four adult sooty mangabey monkeys (*Cercocebus torquatus atys*) were used in these experiments. Operations were performed by accepted neurosurgical techniques and postoperative

* Aided by a grant from the Fluid Research Fund, Yale University School of Medicine.
† Now at Department of Psychiatry, Bellevue Hospital, New York, N. Y.

observations were made daily at first and at intervals of two or more days as the animals' neurological status became more nearly static. Gross and microscopic examination of the nervous system was carried out post mortem.

This phenomenon of paralysis in flexion was observed, by chance, in an experimental study of spasticity. These four animals which developed flexion paralysis were compared with a group of other monkeys with cortical lesions elsewhere, which showed paresis,—either spastic or flaccid, without the flexor attitude in the lower extremities.[17]

EXPERIMENTAL DATA

Abstracts of the protocols of the experimental animals follow.

Experiment 1. (R.S. 28) Male sooty mangabey age ca. 4 yrs. (wt. 6.8 kg.). Bilateral ablation of areas 6 and 4s. Immediate flexion paralysis. Death on 2nd postoperative day from trauma.

Operation May 14, 1943. Under sodium amytal anesthesia a large bone flap was reflected and a bilateral ablation of area 6 and the greater part of area 4s was performed.

Postoperative Notes. 1st day. During the night the animal had opened the operative incision by pulling its head against the cage side and the bone flap had been displaced. It was quite drowsy and lay in its cage with legs and arms tightly flexed, grasping the cage side with both hands. The opening was repaired and sulfathiazole was dusted into the wound.

2nd day. The animal went rapidly down hill and died.

Autopsy. Lacerations of the pole of the right temporal lobe and of the left parietal cortex were found. There was no gross evidence of meningitis. The convolutions were somewhat flattened. Other organs were grossly normal.

Summary. Reflex grasp, paresis and flexion pattern appeared bilaterally immediately after operation. No other observations were possible because of postoperative cortical trauma.

Experiment 2. (R.S. 29) Male sooty mangabey (wt. 6.8 kg.). First operation: Bilateral ablation of areas 6 and 4s. Paresis in flexion and tremor of all four extremities. Second operation: Ablation of left areas 2, 5 and 7. Contralateral temporary diminution in spasticity.

First Operation May 20, 1943. A large bone flap was reflected and a bilateral ablation of area 6 and the anterior part of area 4s was performed.

Postoperative Notes. 2nd day. The animal lay on its belly with both thighs flexed, adducted and internally rotated. The knees were partially flexed. There was piloerection, immobility of the face, slowness of movement and reflex grasp in all extremities. A fine tremor accompanied movement.

4th day. There was little change. Voluntary movement was performed only grossly in the arms and was greatly impeded by reflex grasping. Posture was unchanged except that the animal was lying on its side. Resistance to passive extension was increased slightly in both legs; tremor continued.

Interval Note. On the 5th day alternating movements of the legs were performed when the animal was supported and dragged along the floor but these soon disappeared. It could neither stand nor walk and the flexed posture of the legs was maintained. Atrophy rapidly appeared in the legs. Knee jerks were equal and active and forced grasp and Rossolimo were present bilaterally. Resistance to passive movement was increased in all extremities but this was slight in the legs and on extension only. Tremor continued.

Second Operation June 2, 1943. The bone flap was reopened and areas 2, 5 and 7 were removed from the left side.

Postoperative Notes. 2nd day. Posture and movement were essentially unchanged. Resistance was met in trying to extend the legs and to flex and extend the arms. The resistance was more marked on the left side.

5th day. The animal lay on the floor of the cage and could neither stand nor sit up. Posture was unchanged. Resistance to passive manipulation was marked in all extremities and was most marked on the left side. Only grasping movements were performed by the hands.

8th day. There had been no change.

10th day. The difference between the two sides was still definite but much less marked. There was extreme resistance to extension of the legs. Atrophy was severe.

14th day. Resistance had equalized again and was extreme against extension in the legs. There was tremor accompanying movements of the arms and moderate resistance in the arms. Placing responses had returned and the animal could grasp quite well with the toes but movements of the leg and thigh were not observed. Flexion in the lower extremities remained. On this day it was killed because of diarrhea and because it had developed pressure sores on its legs.

Autopsy. Nothing unusual was found in any of the viscera. There were numerous decubitus ulcers on the legs. The brain weighed 112.5 gm.

Anatomical Notes. The frontal lesions bilaterally were confined to the gray matter of areas 6 and 4s and extended to the cingulate gyrus in the midline. Adjacent cortex was not involved in the ablation or by secondary changes. The corpus callosum had been injured by the right ablation. The basal ganglia were grossly intact. The parietal lesion on the left did not involve area 4 or subcortical structures. Subsequent histological examination confirmed these findings. It further revealed scattered and sparse, but definite degeneration in the sciatic nerves.

Summary. A large male mangabey, following bilateral removal of areas 6 and 4s, showed reflex grasp, increased resistance to extension of all extremities and a posture of flexion, adduction and internal rotation of the lower extremities and flexion of the upper extremities. Posture was not altered by the removal of left parietal areas two weeks later but extension resistance on the right seemed slightly diminished temporarily. Tremor occurred in all four extremities on movement or on static maintenance of posture.

Experiment 3. (R.S. 25) Male sooty mangabey. Operation: Bilateral ablation of areas 6 and 4s. Flexion paresis and tremor bilaterally.

Operation April 26, 1943. A large bone flap was reflected under amytal anesthesia and a bilateral excision of area 6 and the anterior part of area 4s was performed.

Postoperative Notes. 1st day. The anterior portion of the operative incision had been broken while the strong reflex grasp pulled the animal against the cage; this was repaired. Later in the day it was observed that although alert, he could not right himself or stand.

2nd day. The animal lay on its left side with both legs flexed at the knee and thighs flexed upon the abdomen. The arms were partially flexed and the fists clenched. No voluntary movements of arms or legs occurred. Resistance to extension was present in the arms but the legs could be moved freely.

6th day. The picture was unchanged except that resistance to passive extension of the lower extremities was now increased. The knee jerks were 2+.

7th day. Gross voluntary movement of the arms was manifest and resistance to passive extension of the legs seemed most marked on the left. The flexion, adduction and internal rotation in the lower extremities were maintained. Fine tremor was present with movement.

Subsequent Course. Great atrophy occurred in the legs and hyperflexion continued. Knee jerks were 4+bilaterally. Resistance to passive extension became extreme as did atrophy. Tremor on movement continued.

24th day. The animal was sacrificed and autopsy was performed. Decubitus ulcers were present on both buttocks and the extensor surface of the legs.

Anatomical Note. On the surface and on section of the brain nothing except the operative lesions were seen. These were confined to areas 6 and 4s. There was no involvement of subcortical structures. Histological examination confirmed these findings. In the cord, slight degeneration was found in the pyramidal tracts.

Summary. Following bilateral ablation of areas 6 and 4s this adult mangabey showed limited patterns of movement. There was reflex grasp and tremor; flexor posture of the arms; flexion, adduction and internal rotation of the legs, increased resistance to extension of both arms and legs and extreme atrophy of the legs.

Experiment 4. (R.S. 35) Maturing female sooty mangabey (wt. 4.15 kg.). First operation: Bilat-

eral ablation of areas 6 (mesial part). Flexion paralysis with partial recovery. Second operation: Ablation of left areas 3, 1, 2 and 5. Little change.

First Operation July 21, 1943. Under amytal anesthesia a large bone flap was reflected and midline ablations of the mesial part of area 6 were made bilaterally.

Postoperative Notes. 1st day. The animal lay, ventral side down with all extremities flexed, the thighs adducted and internally rotated. Food could not be carried to the mouth; standing and walking could not be performed. Forced grasp was present in all extremities; knee jerks were active. All extremities showed increased resistance to passive extension.

2nd day. There was no change except that resistance to passive flexion as well as extension was now present in the legs.

4th day. A pressure sore had appeared on the left knee and resistance to passive movement of that leg was greater than on the right.

6th day. The animal was now able to move its toes when the dorsum of the foot was brought in contact with the under surface of the table-top (placing response[2]).

13th day. Movements in the upper extremities had improved. Resistance to extension of the legs was extreme.

Interval Note. During the next two weeks movement in the upper extremities showed further improvement; movement was observed in the toes more frequently; the animal sat up, walked clumsily with a scissors gait and finally began to climb.

Second Operation August 18, 1943. The left postcentral gyrus was excised under amytal anesthesia through the old bone flap.

Postoperative Note. 1st day. Posture and movement were but slightly changed by operation. No change occurred until time of death.

September 28, 1943. The animal was sacrificed and autopsy was performed.

Anatomical Note. Brain weight: 93.1 gm. There were bilateral midline lesions of area 6 extending neither into area 4s nor the lateral part of 6a. The corpus callosum was injured in the depths of the excavations. On the left there was ablation of the postcentral gyrus. Marchi sections showed moderate degeneration in pyramidal tracts of the cord.

Summary. Following simultaneous bilateral ablation of the medial part of area 6 this animal showed extreme paresis in all extremities, inability to stand or walk, flexion of all members and adduction and internal rotation of the thighs. Forced grasp was present, knee jerks were active. After the left postcentral gyrus was removed there was but slight change.

DISCUSSION

A brief examination of some features of this syndrome reveals several significant points.

1. *Onset.* The attitude of flexion, adduction and internal rotation in the lower extremities became manifest as soon as the animal recovered from anesthesia and thus may be considered immediate in onset. This observation is important in considering the genesis of the flexion reflex pattern because it is not in harmony with the view that the posture represents a bilateral flexion reflex caused by painful pressure sores. The latter may, however, be operative in maintaining or accentuating the flexion after it has been established. Contractures, also, can have no part in development of this posture.

2. *Involved Muscles.* The adductors and flexors of the arm, the flexors, adductors and internal rotators of the thighs and the flexors of the legs were the muscles that showed contraction. Attempts passively to extend arms and legs were met with increased resistance. All extremities were paretic but the legs were more severely involved than the arms. The pattern was not modified by the position of the animal since it was present when the animal lay

on its belly or on either side, when held in the sitting posture, or when suspended. It was not, therefore, the mechanical result of position in space.

3. *Tremor.* Voluntary movement of the extremities was accompanied by coarse tremor, accentuated by excitement. This occurred without damage to subcortical gray matter and must therefore be attributed to cortical injury. It was as marked in No. 4, in which only the mesial part of area 6 was removed, as in the other three animals. Tremor is mentioned here as another instance of its appearance after a purely cortical lesion and it in no way differed from the tremor described elsewhere following *seriatim* removal of these same areas in monkeys and chimpanzees.[9]

4. *Atrophy.* Muscular atrophy in the lower extremities was early in onset and extreme in degree. It was more severe than that seen in spastic paralysis, following unilateral removal of area 6, but can be accounted for by the almost complete immobility of the legs in the present instance. The early degeneration found in one sciatic nerve examined might also be a contributing factor in the atrophy. Its cause is unknown, but it could be due either to nutritional defect or to pressure.

5. *Recovery and Residue.* A notable feature of the flexion paralysis syndrome as produced in these experiments is that movements of the toes and feet reappeared while legs and thighs still remained flexed and immobile. The one animal that regained the use of its legs was left with residual flexion, adduction and internal rotation and walked, as a result, with a peculiar gait, knees together and feet apart.

6. *Reflexes.* As would be expected, forced grasp occurred in all extremities and Hoffmann's and Rossolimo's signs could be elicited. Knee jerks were normal or, more frequently, hyperactive. The latter suggests that increased extensor activity was present but masked or overpowered by great flexor overaction.

The reflex grasp, present in all four extremities, was in most respects similar to that described by many previous authors as the result of damage to area 6.[5] There are, however, several characteristics usually associated with reflex grasping which did not appear here. When reflex grasping occurs as the result of bilateral removal of *areas 4 and 6* it appears as a reflex flexion of the fingers and toes which is clearly affected by change in the position of the animal with respect to gravity. There is always then a relative increase in the reflex grasp in uppermost hand and foot and a decrease in undermost. This is accompanied by a relative extension of the undermost and flexion of the uppermost extremities. Although the grasp itself was thus modified in the present animals, there was little or no change in the flexion posture or in resistance to passive manipulation as a result of change in space. Also, although the reflex grasp was transitory, as it always is from lesions of area 6, the flexor posture was maintained in the two animals which lived long enough beyond the time when reflex grasping had disappeared.

It is to be expected, from existing knowledge of the specific functions of area 6, that postural changes and reflex grasp should be greatest when there

is a *simultaneous bilateral* extirpation because of the known bilaterality of function of this region. That the marked flexor posture had not been observed following *seriatim* ablation of area 6 may be due to the recovery of function that takes place between two such operations.

In this connection the relation of the midline tissue of area 6 should be stressed and *Experiment 4* cited. In the first three experiments an effort was made to remove all of area 6 including the tissue from the midline surface to the cingulate sulcus. When the striking picture of flexion and tremor appeared in three successive animals with this lesion it was felt that a smaller lesion might have the same effect. Therefore, in Experiment 4, only the

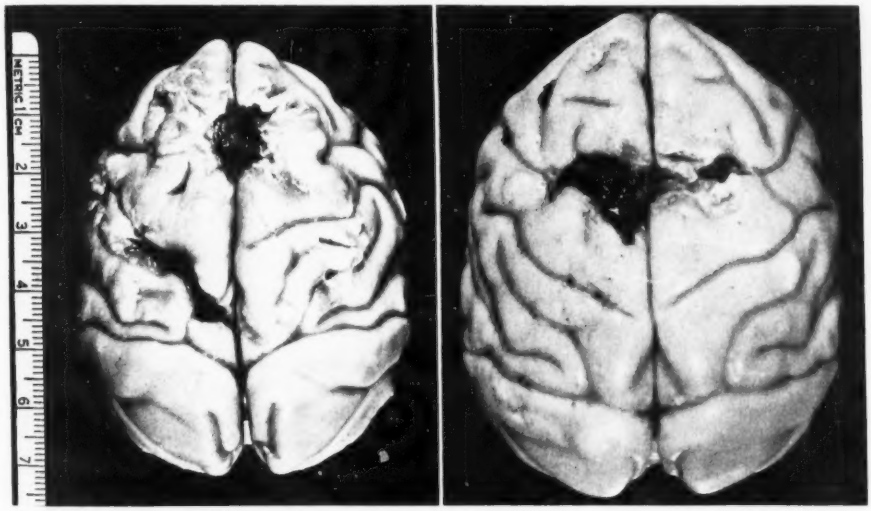


FIG. 1. Brains of two monkeys. *Left* shows ablation of mesial part of area 6 and left postcentral lesion (Expt. 4). *Right* shows bilateral removal of area 6 (Expt. 3).

mesial portions of the lateral surface of area 6 were removed together with all tissue to the cingulate sulcus (Fig. 1). In this animal the tremor and flexor postures were as marked as in the other three, except that the paresis was less extreme, thus enabling the animal in the space of a few days to walk about.

Indications are then, from these experiments, that the strong flexor posture accompanied by forced grasping is produced by lesions of the mesial surface, and that ablations here more greatly influence flexor posture than paresis. The posture may in this connection be thought of as a part of the complex reflex pattern of involuntary grasping.

The tendency to maintain a flexed posture may be compared with the extensor tendency seen in decerebrate rigidity. Both are so strong that they overcome, in part at least, all stimuli which would otherwise produce

changes in postural pattern such as righting. By the addition of area 4 to ablation of area 6 an equalization of extensor and flexor mechanisms is produced, because the monkey following bilateral removal of areas 4 and 6 not only develops changes in resistance to passive flexion and extension with change in position in space, but also has a spasticity in which resistance is more nearly equivalent in the flexors and extensors.

SUMMARY

1. Simultaneous bilateral removal of areas 4*s* and 6 or of area 6 produced paresis in flexion in four mangabey monkeys.

2. This was associated with reflex grasping and with increased resistance to passive manipulation in all extremities, greater on extension than on flexion.

3. Tremor, coarse and present on movement, occurred as the result of this purely cortical lesion.

4. It is suggested that the reflex flexion pattern is an extrapyramidal release phenomenon and that it is functionally related to the pattern of reflex grasping.

REFERENCES

1. Alajouanine, T. Sur un type de paraplégie en flexion d'origine cérébrale. *Ann. Méd.*, 1923, *13:* 243–275.
2. Bard, P. In: *Macleod's physiology in modern medicine.* St. Louis: C. V. Mosby Co., 1941, 9th ed., 1256 pp. (see p. 227).
3. Daniels, L. E. Paraplegia in flexion. *Arch. Neurol. Psychiat., Chicago,* 1940, *43:* 736–764.
4. Demange, E. Contributions à l'étude, 1. des tremblements prae- et posthémiplégiques, 2. des hémiplégies bilatérales par lésions cérébrales symmétriques. *Rev. Médecine,* 1883, *3:* 371–404.
5. Fulton, J. F. The interrelation of cerebrum and cerebellum in the regulation of somatic and autonomic functions. (Harvey Lecture.) *Medicine,* 1936, *15:* 247–306.
6. Herman, W. A case of paraplegia in flexion of arteriosclerotic origin ("Contracture des atheromateux" of Demange). *Psychiat. neurol. Bl., Amst.,* 1926, *30:* 32–44.
7. Hines, M. The "motor" cortex. *Johns Hopk. Hosp. Bull.,* 1937, *60:* 313–336.
8. Holmes, G., and Sargent, P. Injuries of the superior longitudinal sinus. *Brit. med. J.,* 1915, *ii:* 493–498.
9. Kennard, M. A., and Fulton, J. F. Age and reorganization of central nervous system. *J. Mt. Sinai Hosp.,* 1942, *9:* 594–606.
10. Lejonne, P., and Lhermitte, J. Les paraplégies d'origine lacunaire et d'origine myélopathique, chez les vieillards. *Arch. gén. Med.,* 1905, *196:* 3009–3027; 3073–3086.
11. Marie, P., and Foix, C. Paraplégie en flexion d'origine cérébrale par nécrose sous-épendymaire progressive. *Rev. neurol.,* 1920, *36:* 1–8.
12. Van Bogaert, L., and Ley, R. Contribution à la connaissance de la paraplégie en flexion, type Babinski, d'origine cérébrale. *J. belge Neurol. Psychiat.,* 1926, *26:* 547–556.
13. Verhaart, W. J. C. Some clinical and anatomical observations on the "Paraplégie en flexion" and related motor disturbances. *Proc. Acad. Sci., Amst.,* 1929, *32:* 961–972.
14. Verhaart, W. J. C. "Paraplégie en flexion" in consequence of a decerebration above the nucleus ruber. *Psychiat. neurol. Bl., Amst.,* 1930, *34:* 33–41.
15. Verhaart, W. J. C. The flaccid hemiplegia of cerebral origin. *Psychiat. neurol. Bl., Amst.,* 1937, *41:* 211–217.
16. Walshe, F. M. R. The physiological significance of the reflex phenomena in spastic paralysis of the lower limbs. *Brain,* 1914–15, *37:* 269–336.
17. Welch, W. K., and Kennard, M. A. The relation of the cerebral cortex to spasticity and flaccidity. (In preparation)

MICROCEPHALUS SECONDARY TO BIRTH TRAUMA*

EDGAR F. FINCHER, M.D.

Department of Surgery, Emory University School of Medicine, Atlanta, Georgia

(Received for publication May 17, 1944)

THERE HAS BEEN little or no surgical interest in microcephalus since the turn of the century. It seems a bit unusual with the progress and contributions in the field of neurologic surgery that no one has attempted a revival of or any improvements on the surgery of the 1890's in behalf of this hopeless group of children. With the idea of possibly helping these babies by surgery, a review of the English literature was made by the author in 1935. This revealed a goodly number of articles dealing with the effects of irradiation upon the foetus, with resulting microcephalus. Many of these publications were controversial but the weight of evidence was that there were arrested developmental cerebral changes in these infants and as such the group did not invite any surgical interest.

Freeman[4] in 1927 reported in detail the histologic changes in four cases of microcephalus and these were discouraging for any optimum surgical possibilities. He found "a disordered fat metabolism as a distinctive feature" and "the absence of any inflammatory vascular and degenerative changes striking." Eley[3] in 1933, in a review of neurologic conditions in children, was most discouraging in that "the treatment of this disorder (microcephalus) is ineffective." He felt there could be little doubt "that trauma to the brain must be related to the production of microcephalus." In support of this statement he cited the "frequency of a history of intracranial hemorrhage as a result of trauma or secondary to hemorrhagic disease of the new born" in these children. In 1926 Brushfield and Wyatt[1] supplied an excellent statistical study on six per cent of 1545 mentally defective children: twelve per cent of these defectives had cranial circumferences smaller than normal, but they felt that only six per cent were true microcephalics. The measurements as reported by these authors have been followed in diagnosing the microcephalics to be discussed in this communication, although a disproportion of more than 4 centimeters between the greatest circumference of the baby's head and chest measurements at the nipple line has been a practical criterion for such a diagnosis. These same authors[2] in 1927 gave the autopsy findings in 10 cases, and in every instance "the meninges showed signs of chronic inflammatory changes . . . the dura was thickened and sometimes adherent to the pia arachnoid" microscopically . . . "the cerebral cortex showed a definite paucity of neurones; in the precentral gyrus for instance there were areas almost devoid of healthy pyramidal cells, etc. . . . Some brains under consideration showed definite evidence of a slight degree of atrophic sclerosis affecting both hemispheres." Recalling the numerous in-

* Presidential Address, 13th Annual Meeting of The Harvey Cushing Society, New York City, May 17, 1944.

stances in which dural-arachnoidal adherences in cases of tumor have been mistaken as the sole cause of the clinical symptoms of increased intracranial pressure, and the earlier explanations of pachymeningitis hemorrhagica on inflammatory bases, it occurred to mind that the chronic inflammatory changes described by Brushfield and Wyatt might well have been the result of subdural bleeding from birth trauma.

Lannelongue[6] in 1891, before the 5th French Congress of Surgery, reported his results in 25 cases of craniectomies on microcephalics. He referred

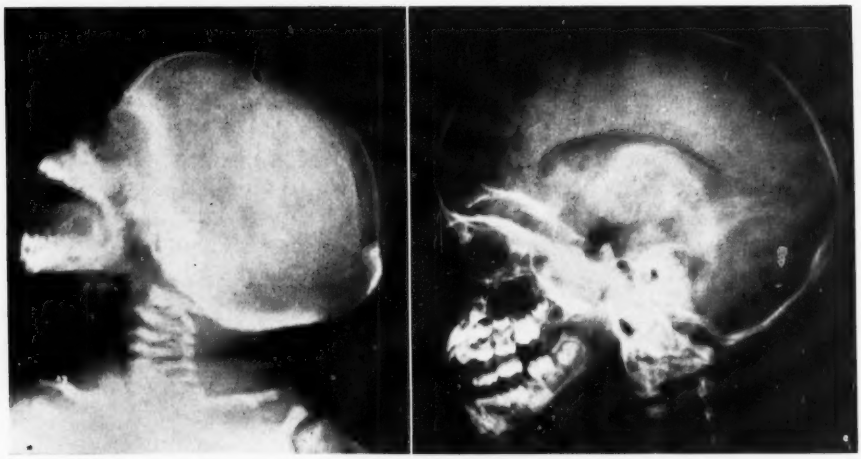


FIG. 1 (*left*). Radiologic depictions of any changes other than premature bony closures excluded certain microcephalics for trephine exploration.

FIG. 2 (*right*). The rather consistent failure of air to enter the subarachnoid spaces in certain microcephalics might possibly be explained by the presence of the subdural membranes.

to them as obstetrical compressions due to forceps deliveries or difficult labor. He advocated linear or flap craniectomy and "detached the dura mater and allowed it to remain untouched." In the 25 cases "the majority were improved both intellectually and in their ability to walk." In this same year Keen[5] reported 8 cases—3 of his own and 5 others whose records were furnished by his contemporaries. In none of these was the dura opened. One patient followed by Keen for a year "certainly improved steadily and considerably." Wyeth (1891)[10] noted that intelligence had greatly increased in a month following a bony incision. In 1900 Naylor[7] sacrificed a large parietal flap without opening the dura and within a week noted improvement in the general spasms and that the spasm of the eyeball was less severe in extent and frequency. After 3 weeks his patient was moving the formerly spastic right arm and leg "quite freely." The first report in which the dura was opened was by Stiles[8] in 1901 (linear craniectomy). "The object of this was to prevent the subsequent obliteration of the artificial suture by the formation

of new bone, which we know develops to a much greater extent from the dura than from the pericranium." Eight weeks after Stiles had operated, the cranium on the side of operation was "perceptibly larger than the opposite side."

These surgical reports were encouraging. The pathologic changes in Brushfield's studies were not in every instance beyond the hope that with earlier surgical interferences certain possible secondary changes in the microcephalics might be prevented. The selection of patients in the present series was limited to those whose births were definitely pathologic, for certainly the hereditary group[9] and those of normal birth were likely to have developmental defects. The next consideration was the age for investigation. Of course, the earlier the better if it were secondary damages that were to be obviated, but in the earlier cases, using physical measurements, skull disproportions were too minimal to be accurate about the true existence of microcephalus. In the first six months of life the circumference of the head is increased by three inches and it was usually after this age or later that the abnormally small heads were recognized, so that the earliest investigative ventures were carried out in babies past six months of age.

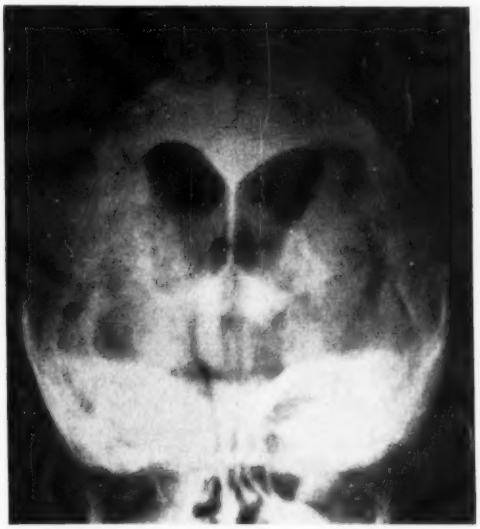


FIG. 3. It is most likely that the ventricular enlargements in this case were compensatory, although posterior fossa hematogenous membranes have been revealed in 2 cases with obvious hydrocephalus.

The presence of definite bilateral optic atrophy and objective evidence of blindness, irrespective of a history of birth injury, was used as a definite contraindication for any investigative or surgical consideration. Plain X-ray films of the skull when they revealed any changes (Fig. 1) other than premature bony closures were utilized in excluding further investigations. In pneumo-encephalographic experiences in an older group of microcephalics prior to 1935 various ventricular enlargements and deformities had been noted—in this same group the failure to visualize the subarachnoid spaces (Fig. 2) occurred in a greater percentage than had been the average in a comparable group of children who were not microcephalics. It is possible that chronic meningeal changes prevented subpial air entrance, and it was the proposal of introducing the air directly into the ventricles by way of the anterior horns that revealed the existing subdural changes. When these pathologic changes were more grossly

reviewed at a subsequent linear craniotomy, it was obvious that subarachnoid air, had it been disseminated over the hemispheric surfaces, would have unlikely depicted the presence of a pathologic subdural membrane. In subsequent cases spinal air introductions have been carried out either pre- or postoperatively for investigative purposes and not in the hope of depicting the extra-cortical lesion. It is likely that preoperative encephalographic studies (Fig. 3), should the ultimate surgical results justify their indications, form a definite basis for the proper selection of these cases. In the cases to be discussed in this communication trephine exploration has been the means of demonstrating or excluding any subdural pathology.

OPERATIONS

There have been 17 patients operated upon. In five cases trephine exposures were made; no extra-cortical pathology was seen and the scalp was closed. In 12 instances a subdural membrane was exposed and the trephine exposure was extended to a linear temporo-frontal craniotomy; eight of these patients have had subsequent procedures on the opposite side of the skull, so that bony and dural sacrifices, from zygoma to zygoma across the vertex, have been effected. In no instance where a membrane was uncovered on one side has there been a failure to expose a similar change over the opposite hemisphere. In one of the four cases in which only a unilateral exposure was carried out there was a respiratory fatality six hours after operation. In another less than a month has lapsed since the initial operation. In the third there was such obvious cerebral atrophy (external hydrocephalus) that a second procedure was not considered. In a three-months observation period the head circumference remained the same and the frequency and character of the convulsions remained unchanged. In the fourth case there occurred an increase of 1 centimeter in the head circumference in a four-months lapse of time from the unilateral operation. The chest circumference in this period had increased 5 centimeters. The decerebrate attacks had not been influenced by the surgical efforts and the decompression area was constantly a centimeter below the normal skull contour level.

In the eight cases in which bilateral operations have been carried out the second procedure was based on several requisites: (1) that at the time of the primary procedure the exposed hemisphere did not exhibit any grave gross abnormal changes; (2) that the convulsive seizures had positively been influenced, with either a decrease in frequency and severity or evidence that they were firing primarily from the opposite cortex; (3) that signs of decerebration, when present before exploration, had been materially lessened; and (4) a measurable increase in head circumferences in three cases where symptomatic evidence of improvement was feebly established.

CLINICAL HISTORIES

The clinical histories of the children who have these hematogenous subdural membranes are all so similar and the seizures which have been per-

sonally observed in almost every instance are so much alike that a clinical picture can be described which, with a few minor individual variations, is typical of all of them. They all have been first-born. The deliveries have been pathologic, with a short or difficult labor, or the use of pituitrin or forceps, and more than half of the infants required artificial respiration. General convulsive seizures occurred within the first two or four days of life. Eight of the 12 had bloody spinal fluid on lumbar punctures. Symptomatic treatment was instigated, and by the time the mother's post-obstetric recovery was assured the baby's symptoms had subsided and the maternal fears of a handicapped child were abated.

At the age of two to three months focalizing irritations began. The patterns of progress in these attacks were not always the same: first one side

FIG. 4 (*left*). This 9-months old baby had all 4 cranial physical characteristics of microcephalics.

FIG. 5 (*right*). This 4-months old baby girl had only the over-riding anterior sutures and a bifrontal narrowing. Facial features and expressions were good and the posterior contour of the skull could not be classed as abnormal.

was involved and then the other—sometimes the mother's observations were those of clonic seizures of the head and eye—the initial onset would be in one extremity, then another. Although the irritations may have been bilateral, severe generalized convulsions occurred in only two cases. Sedatives played little role in controlling the focal irritative phenomenon, and 20 to 30 attacks a day were recorded in some of the mothers' diaries.

A difficulty in the baby's ability to grasp objects and to hold up its head at three to four months of age was a characteristic paternal observation in almost every instance. In the children over eight months old an early fontanelle closure had been noted by the parents in the majority of cases, their

observations being that there was no fontanelle at three months of age, or complete disappearance before the age of six months.

The attacks of these children occurred with such frequency that it was possible to observe many of them prior to trephine exploration. There are two characteristics: (1) Jacksonian seizures, mild in character, definite in pattern and short in duration; (2) spontaneous rigidities, either quadra-extensor in character or unilateral extensor and crossed flexor types. While physical measurements and early fontanelle closures have been the criteria for classing these children as microcephalics, not all of them have the birdlike appearances, the flattened occiputs and the two marked angles (1) of the facial center and (2) at the vertex of the head. Most of them have had one and many two of these four physical characteristics of the microcephalic group (Figs. 4 and 5).

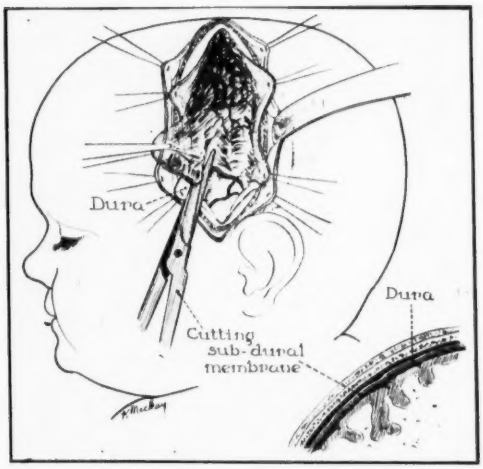


FIG. 6. Artist's concept of the linear craniotomy and the subdural pathologic changes.

METHOD OF OPERATION

The surgical procedure used in these cases was a linear craniotomy from the zygoma to the vertex across the longitudinal sinus. A 3-centimeter sacrifice of the skull was made and the dura and its attached membrane removed as this bony exposure permitted. Care was exercised against opening the arachnoid (Fig. 6).

PATHOLOGY

The subdural pathology revealed on these exposures has been uniformly the same and this rather than the surgical technique or results of operation may well be the only justification for this publication. In the initial trephine exposure the dura is likely to be thickened in comparison with the dura in cases of tumor or in traumatic craniotomies in babies. Free cerebral pulsations are not grossly obvious. When the dura is opened one encounters a greenish or purple-tinged membrane, in direct contact with the inner dural surface. Its appearance is very much that of an older chronic subdural hematoma membrane, and its adherence to the dura is identical. Using a small grooved director or a small dissecting blade this membrane can be freed from the dura without any bleeding. On cutting through this friable membrane its depth will approximate that of the dural thickness. Although in three specific instances a thinner transparent pial membrane was demon-

strated as a separate structure, no collection of old free liquefied blood was seen in any of the 20 exposures. As the dura is opened toward the temporal lobe the pathologic lesion is likely to thin out and disappear beneath the temporal bone. On extending the dural exposure to the longitudinal sinus the membrane increases in thickness. One wonders from this constant finding if the origin is from a torn bridging vein that drains into the sinus or from a tear in the sinus with an escape of blood outside the pia arachnoid.

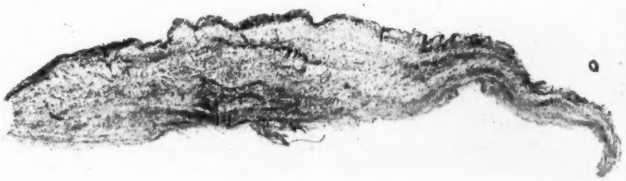


FIG. 7. Section from a membrane in a baby 4 months of age. (Hematoxylin-eosin × 6)

The microscopic characteristics of these subdural membranes are similar to those of pachymeningitis hemorrhagica and are shown in detail in the microphotographs (Figs. 7, 8, and 9).

RESULTS OF OPERATIONS

The surgical results in three instances have been very striking. The dominating Jacksonian seizures were promptly minimized when the first

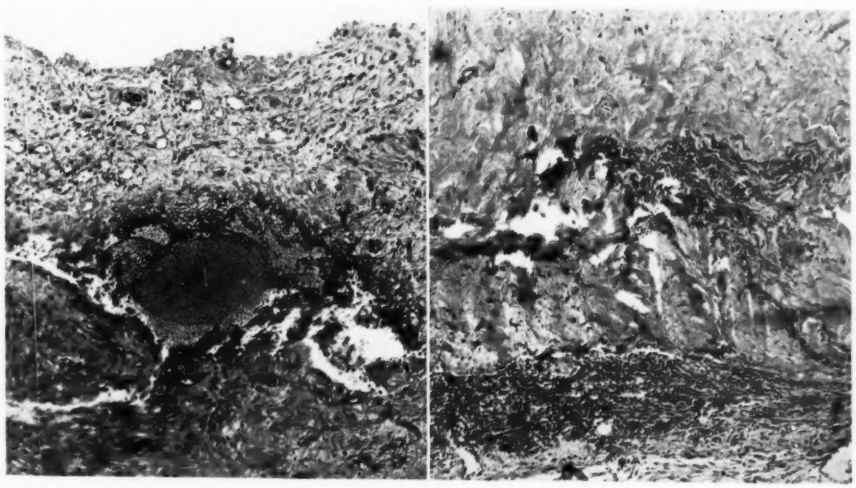


FIG. 8 (*left*). Same specimen as Fig. 7. All of the histologic studies have been characteristic of the changes in chronic subdural hematomas. (Hematoxylin-eosin × 75)

FIG. 9 (*right*). This was removed when the baby was 3 months of age. (Hematoxylin-eosin × 75)

operation was performed. The opposite side then dominated until the second procedure was carried out.

Case I (3523). This is the oldest child in the series. At the age of 8 months she was operated upon in 1935 by a right-sided procedure because of dominating left spasticities (10 to 30 attacks per day). There was an increase of $1\frac{1}{2}$ cm. on hemicircumferential skull measurements within 30 days after operation. The mother and attending nurse had observed no left-sided attacks during this period. The left craniotomy was performed 6 weeks after the first one. There were no Jacksonian seizures during the postoperative hospitalization and when she returned for observation 2 months later the mother and nurse reported an absence of any jerking attacks or phenomenon suggesting decerebrate seizures. The head circumference on this date had increased $3\frac{1}{2}$ cm. from the initial measurements, which at that time were 5 cm. below normal.

Seen a year after the second operation there had occurred, according to the mother, an occasional flexor attack involving the right arm, and in walking with support there was a suggestive equinovarus of the right foot. She subsequently learned to walk, and to talk at the age of 3 years.

At 4 years of age her cerebration was quite below normal; she had been trained to good bath-room habits; the equinovarus deformity was much more in evidence in her locomotion; and her mother described attacks of a spastic character involving her entire right side. These were said to be transient in duration and as frequent as 10 per day and as infrequent as once a month.

At 6 years of age she was entered in a school for defectives. The right-sided spasticities continue as transient seizures, but on last report she had had no generalized convulsions and no further Jacksonian attacks.

Case II (3652). The second oldest case in the bilaterally operated group had a similar follow-up course. His original dominating Jacksonian features involved the muscles of the left chest and abdominal wall, at times being so continuous as to result in a body torsion to that side. He was first seen at the age of 8 months, with a 7-cm. disproportion in the size of his head. Following the initial operative procedure the left-sided symptoms were reduced to an occasional twitching with no status seizures.

He was seen at intervals during the successive 6 months. He was able to hold up his head and move it freely within a month after operation. Four months after operation he could sit alone, but when placed on his abdomen he was unable to turn himself over. His attacks were 1 to 2 per day, were momentary, and from the mother's description were more like decerebrate seizures with the right extensor pattern dominating. The circumference of the head increased $1\frac{1}{2}$ cm. in this 6 months. The left linear craniotomy was done at this time.

A month later, having had no spastic upsets during his immediate postoperative hospital convalescence, his mother wrote that he had on first awakening each morning some attacks that simulated his former decerebrate seizures but that there was no domination of one side over the other. A year from the first operation he had learned to take steps with support, and had learned one or two baby words. He continued on awakening to have rigidity phenomena. He died at the age of 20 months from pneumonia, undoubtedly an act of mercy.

Case III (36211). This child, operated upon in 1936, had a head that was $4\frac{1}{2}$ cm. smaller than normal measurements. He was 7 months of age when first seen. Permission for operation was not given by the parents until the child was readmitted to the hospital at 11 months of age. The head circumference had increased 1 cm. in this interval, while the chest circumference at the nipple line had not changed. He had generalized convulsive seizures beginning with a rotation of the head and eyes to the right side. A right-sided procedure was carried out. There was a moderate external hydrocephalus.

He had one attack during his 10-day postoperative stay in the hospital. For $2\frac{1}{2}$ months his convulsions were at 12 to 14 day intervals and he would have only one attack on these

days. He then began having as many as 6 per day. These continued, and when seen the child was definitely idiotic in appearance, more spastic than relaxed, and the spasticities were greater in the right extremities. Eight months after the first surgical procedure the character of the seizures had changed from generalized convulsions to momentary spastic attacks precipitated at will with loud noises; the right arm and leg were obviously more involved than the left extremities. A month later the left craniotomy was done.

The parents reported 2 months later: "His spells don't bother him very much but every day or so he has a very light one." Fourteen months after the second craniotomy the baby was still idiotic. He could sit alone, had no words in his vocabulary, and "the spells have left

FIG. 10 (*left*). The left temporal bulge is not to be mistaken as evidence of cerebral expansion. This photograph was taken 6 weeks after the craniotomy, at which time the arachnoid was accidentally opened, and part of the temporal expansion is the result of fluid escape under the scalp exposure.

FIG. 11 (*right*). The recent selection of babies has been on the basis of focal irritations, intelligent appearances and freedom from any suggestive spasticities.

him entirely but now and then he will get awfully nervous." He died of pneumonia at 6 years of age, never having learned to walk, feed himself, talk, or cerebrate, but he was free from generalized convulsions during the last 4 years of his life. Permission for autopsy was impossible to obtain.

Case IV (38150). A 7-months-old baby girl began at 2 months of age to have attacks occurring from 6 to 20 times per day. Many of these attacks were observed. They had their onset with a twitching of the right facial muscles, then spread to involve the right side of the tongue, then the shoulder and ended with a spastic extension of the arm. There was a 7-cm. disproportion in the circumference of the head. A zygoma to zygoma incision was made across the vault and the bone rongeured away for a width of $2\frac{1}{2}$ cm. The dura and its attached subdural membrane were sacrificed except over the longitudinal sinus.

She was dismissed from the hospital 2 weeks after operation and one month later the

mother reported 3 to 4 light attacks for that month involving the right eye and mouth, with no spread into the extremity. The child held up its head and turned it decently, had use of her hands and arms in reaching for and holding objects, took certain recognitions of her surroundings, and supported her weight on her lower extremities with assistance. When 5 years of age she could walk unassisted without any frank spasticities, her vocabulary was very limited, her bath-room habits were well established, and transient mild irritative involvement of the right face and eyes occurred on an average of 5 to 6 times a day. She had no generalized convulsive seizures during this time interval.

Cases V, VI, VII and VIII. These children have all been operated upon within the past 12 months. They have been younger and selected with more neurologic care (Fig. 10) than in any of the previous cases. Cases V and VI were 4 months of age. Case VII (Fig. 11) was 5 months old at the time of the initial craniotomy. Case VIII is the youngest and most recently operated upon, having just had the second unilateral procedure. These four patients have not had any generalized convulsions since the initial ones at birth. Focal seizures, even though in some instances initiated in first one part of the body and then another, have all been observed in more than one attack in every case. In these four most recent cases, surgery seems to have had some definite beneficial effects upon the irritative symptoms. The ultimate progress will be routinely followed.

COMMENT

It appears that birth trauma is a definite factor in some cases of microcephaly. The subdural hemorrhagic membrane in these cases is analogous to the membrane of pachymeningitis hemorrhagica of the chronic subdural hematomas in adults. It is possible that this membrane in babies may be a secondary factor in the production of certain cortical histologic changes and might even be a factor in the failure of the cerebrum to expand. Autopsy studies compared with examinations of the cortex removed by biopsies should ultimately shed some light on the first possibility, and further follow-up physical measurements should net some information regarding the second possibility. When one is familiar with the intrinsic cerebral damages resulting from birth injuries one cannot become very enthusiastic in advocating any surgical procedures in these handicapped children, but if something can be done to minimize or prevent secondary damage, one might consider one's efforts more effective.

REFERENCES

1. Brushfield, T., and Wyatt, W. Microcephalic children. *Brit. J. Child. Dis.*, 1926, *23:* 265–270.
2. Brushfield, T., and Wyatt, W. Microcephaly. *Brit. J. Child. Dis.*, 1927, *24:* 24–31.
3. Eley, R. C. Neurologic conditions in infants and children. Critical review. *J. Pediat.*, 1933, *3:* 781–796.
4. Freeman, W. Microcephaly and diffuse gliosis: a clinico-pathological study of four cases. *Brain*, 1927, *50:* 188–215.
5. Keen, W. W. Linear craniotomy (miscalled craniectomy) for microcephalus. *Amer. J. Med. Sci.*, 1891, *101:* 549–555.
6. Lannelongue, O. M. Craniectomy in microcephalus and in children presenting some lack of development, with or without epileptic fits, all of cerebral origin. *Med. News, N. Y.*, 1891, *58:* 473.
7. Naylor, G. H. Linear craniectomy for microcephaly with considerable improvement resulting. *Aust. med. Gaz.*, 1900, *19:* 330–331.
8. Stiles, H. J. Linear craniectomy for microcephalus. *Trans. med-chir. Soc. Edinb.*, 1901, *n.s. 21:* 240.
9. Whitney, E. A. Microcephaly. *Med. J. Rec.*, 1932, *135:* 166–168.
10. Wyeth, J. A. Craniectomy for microcephalus. *Med. Rec.*, 1891, *39:* 232.

THE DIFFERENTIAL DIAGNOSIS OF INTRASPINAL TUMORS AND PROTRUDED INTERVERTEBRAL DISKS AND THEIR SURGICAL TREATMENT*

J. GRAFTON LOVE, M.D.

Section on Neurologic Surgery, Mayo Clinic, Rochester, Minnesota

(Received for publication May 18, 1944)

THE SYNDROME of protruded intervertebral disk has been well established and the high degree of accuracy with which the diagnosis is made, not only by the neurologist and the orthopedist but also by the general practitioner of medicine, speaks well for the high type of medicine and surgery that is being practiced in this country today.

FIG. 1. Back of patient who had undergone, elsewhere, lumbosacral fusion and, six months later, fasciotomy without relief of low back and left sciatic pain of four years' duration. An intradural and extradural neurofibroma was removed from beneath the bone graft, with immediate relief of the patient's symptoms. In this case, lumbar puncture had not been performed prior to the fusion operation. The scar of the fusion operation is indicated between the two arrows on the left, and that of the laminectomy for removal of the tumor, between the two arrows on the right.

In the majority of cases of protruded intervertebral disk, the diagnosis can be accurately made on the basis of the history and physical findings. Many patients, however, present themselves with histories of intractable pain of root type, and these patients require special methods of examination before accurate diagnosis can be made. If diagnostic errors are to be kept at a minimum, and if the best results are to be obtained from therapeutic efforts, the mistake should not be made of considering every intractable low

* Read before The Harvey Cushing Society, New York City, May 18, 1944.

back and sciatic pain as being due to protruded intervertebral disk. It should be remembered constantly that trauma may initiate the symptoms of intraspinal neoplasm just as well as those of protruded intervertebral disk.

It is extremely important, in planning and executing the operation for relief of intraspinal pressure, to know which of the following is indicated:

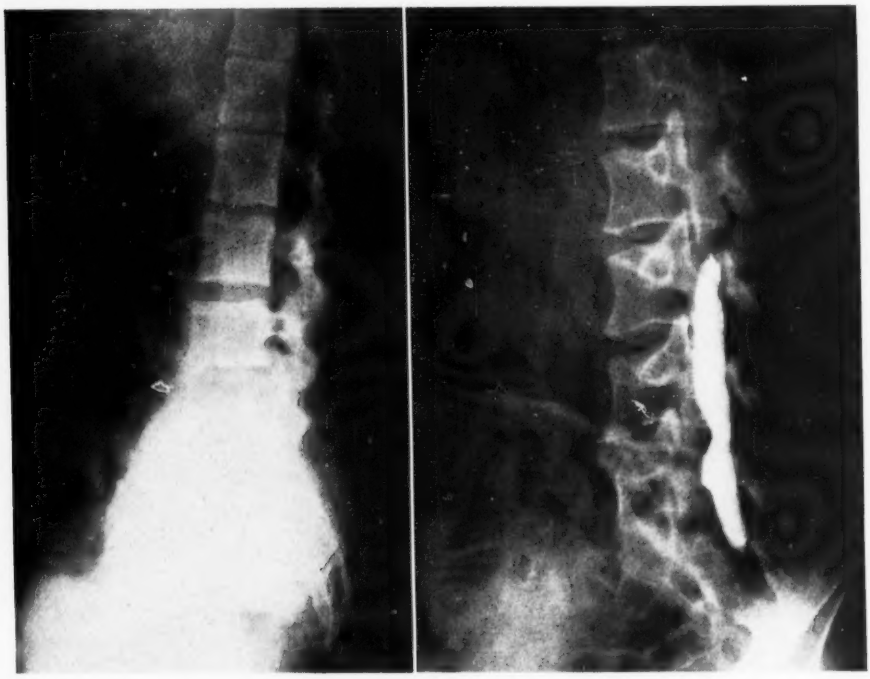


FIG. 2. Lateral roentgenogram of the lumbar and sacral portions of the spinal column after the cerebrospinal fluid had been replaced with air. There is a defect at the fourth lumbar interspace due to a protruded intervertebral disk. The protrusion was so large it had blocked the spinal canal and the air could not get by the block to visualize the lumbosacral space.

FIG. 3. An oblique roentgenogram of the lumbar and sacral portions of the spinal column after injection of lipiodol for roentgenoscopic examination of the spinal canal. There is a defect in the column of lipiodol at the fourth lumbar interspace due to a protruded intervertebral disk.

relatively extensive laminectomy for removal of a tumor or a relatively short operation, with little or no sacrifice of bone, for removal of a protruded intervertebral disk. In compensation cases, likewise, it is important to know prior to operation what the pathologic condition is likely to be and, above all, it is important to avoid an unnecessary surgical procedure whenever possible (Fig. 1).

During the past several years, my neurosurgical colleagues and I at the Mayo Clinic have encountered a great many intraspinal neoplasms mas-

querading as protruded intervertebral disks. In some cases, the mimicry was so great that the differential diagnosis could not be made until the space-taking lesion had been uncovered at the operating table; this, in spite of the fact that every patient suspected of having a protruded intervertebral disk receives, in addition to a general physical examination, an orthopedic examination and a neurologic examination. Moreover, roentgenograms of the appropriate portion of the spinal column are made. Before the patient who has received a clinical diagnosis of protruded intervertebral disk is subjected to surgical operation, he is accorded a diagnostic spinal puncture and his spinal canal is visualized with the aid of a contrast medium. These last two procedures usually will suffice to clear up the differential diagnosis between disk and tumor.

FIG. 4. Postero-anterior roentgenogram of a portion of the lumbar region of the spinal column after introduction of lipiodol into the subarachnoid space. A protruded intervertebral disk was suspected to be the cause of the patient's intractable sciatic pain. The defect opposite the fourth lumbar interspace is due to an intradural neurofibroma, removal of which resulted in relief.

The patient who has a protruded intervertebral disk usually will give a history of trauma or of unusual stress or strain to his back, with subsequent intractable backache or sciatic pain, or both. The pain is usually (in about 85 per cent of cases) intermittent and is not relieved by ordinary measures directed to overcoming the discomfort of myositis, fibrositis, arthritis, or strains of the muscular and ligamentous structures of the back. On examination, the erector spinae muscles are spastic and limping and listing may or may not be present. Spinal motion usually is limited and painful and the straight leg raising test is positive. Neurologic signs usually are minimal and consist, in the main, of diminution or absence of the Achilles reflex, with hypesthesia or anesthesia over a small segment of the surface of the skin. The concentration of total protein in the spinal fluid in two-thirds of the cases will be more than 40 mg. per 100 c.c. but rarely more than 100 mg. Visualization of the spinal canal after injection of air will reveal a defect at the site of protrusion in most cases (Fig. 2). Lipiodol (Figs. 3 and 4), or iodized poppy seed oil, and pantopaque (Fig. 5) give more accurate results in the hands of the experienced roentgenologist than does air, but ordinarily such substances, which require an experienced roentgenologist and a tilting roentgenoscopic table, and which may leave traces of opaque medium in the spinal subarachnoid space, are not essential.

The patient who has a tumor of the spinal cord ordinarily gives a history

of insidious onset of pain that gradually progressed, without intermittency, until he became more or less incapacitated by it. The physical findings frequently are scant but the neurologic signs usually are definite. There may be muscular weakness, atrophy of muscles, reflex changes and definite, and often extensive, sensory changes. In many cases, roentgenologic examination of the spinal column will reveal bony changes indicative of intraspinal pressure. Some of these changes consist in erosion of the vertebral bodies, enlargement of the intervertebral foramina (especially in the presence of dumbbell neurofibromas) and erosion of the pedicles of the vertebrae. On spinal puncture, the fluid often is xanthochromic and practically always contains more than 40 mg. per 100 c.c. of protein. Frequently a subarachnoid block is demonstrable by Queckenstedt's test if the needle is below the level of the tumor. If a contrast medium is used intraspinally, characteristic defects (Fig. 6) are observed and the defect rarely mimics that of the anterior extradural deformity seen opposite the interspace in cases of protruded intervertebral disk.

FIG. 5. Postero-anterior roentgenogram after subarachnoid injection of pantopaque, revealing a defect in the column of pantopaque at the third lumbar interspace due to protrusion of the third lumbar disk, which produced sciatic pain.

Recently, I have collected the data on a group of patients whom I had the opportunity of examining clinically prior to performance of diagnostic spinal puncture, and on whom I subsequently operated. In these cases it was either impossible or very difficult for me to make a differential diagnosis between protruded intervertebral disk and neoplasm prior to the time of lumbar puncture or estimation of concentration of protein in the spinal fluid, or both. As was stated previously, the other neurosurgeons at the clinic have had similar experiences but I am basing my report only on cases of my own since naturally I am more familiar with them and, also, time has not permitted a complete review of all our cases. Nevertheless, all my personal cases are not included, because neither have I had time to review the records of all patients subjected to laminectomy at my hands.

In order to get an idea of the incidence of tumor of the spinal cord masquerading as protruded intervertebral disk, the files were consulted and, during a period when 100 patients were operated on for removal of a protruded intervertebral disk, fifteen other patients underwent operation for removal of an intraspinal neoplasm. Of the fifteen patients who had tumors of the spinal cord, eight presented what is commonly recognized

as the disk syndrome and, if the differential diagnosis had not been made prior to operation, the tumor would have been overlooked or the operative procedure would of necessity have been changed radically from what had been intended at the start of the operation.

REPORTS OF CASES

Case 1. This case is particularly representative of the problem which arises at times when one is asked to see a patient who is suffering from intractable sciatic pain. The man registered on August 22, 1940. The referring physician wrote that the patient was being sent to the clinic because of pain in the back, the thighs and the left inguinal region, the condition having had its onset about a year previously. Quoting further from the letter of reference: "At first there was the complaint of pain in the right lower quadrant, which was suggestive of a mild appendicitis. Later, the pain localized in the left inguinal region. He was seen in consultation by a surgeon who told him that the weakness of the inguinal ring was the cause of the pain. Later the pain included the thighs and back as well as the inguinal region. For the past three weeks it has been especially severe. The discomfort has been most distressing at night and until recently has been relieved by being in the vertical position. Treatment has consisted of heat and massage with salicylates taken internally and occasionally codeine to relieve pain. A course of short wave treatments had no effect. Extraction of one or two abscessed teeth was also done."

FIG. 6. Postero-anterior roentgenogram of the lumbar region of the spinal column after subarachnoid injection of lipiodol. There is a defect in the column of lipiodol characteristic of an intradural neoplasm involving the cauda equina.

On further questioning, we found that during the two months previous to his registration, the patient had had rather severe backache across the sacro-iliac region, with extension of the pain down both thighs, usually stopping at the knees. Occasionally, however, there was slight pain in both ankles. The pain was aggravated by motion, coughing and sneezing. Weather had no effect. Although the pain had been more or less constant for the past two months, at times it would migrate.

Examination. General physical examination gave negative results. Motion of the back was moderately limited. There was tenderness in the lumbosacral region and straight leg raising gave a bilaterally positive result. Roentgenograms of the spinal column were negative. The usual examinations of blood and urine disclosed nothing abnormal. The sedimentation rate, by the Westergren method, was 5 mm. per hour. Results of neurologic examination were entirely negative. Because a protruded intervertebral disk was suspected, a lumbar puncture needle was introduced at the first lumbar interspace and, much to my surprise, the fluid was orange colored and coagulated on standing. There was a complete subarachnoid block. Another spinal puncture needle was introduced at the eleventh thoracic interspace and clear fluid, discolored by traumatic blood, was obtained. There was no block at this level. The head of the table was lowered and an attempt was made to inject air through the upper needle. Pain was excruciating. Very little air could be injected. The impression was that the patient had a spinal cord tumor in the region of the conus medullaris.

Operation. Laminectomy was advised. The operation was carried out with the patient

under ether anesthesia, and the site of operation was between the points of introduction of two lumbar puncture needles. A huge tumor, which arose from the filum terminale, was found to have produced complete block. The cauda equina, which completely surrounded the tumor, was separated from it and the filum terminale was doubly silver-clipped above and below and divided, thus freeing the tumor for complete removal. The dura mater was closed with continuous silk sutures; the wound was closed in layers. One strip of gauze was plicated over the dura and one Penrose cigarette drain above this. Bleeding was unusually sharp and extremely difficult to control. Because of the sharp bleeding and because of the history that the patient had a tendency to bleeding, a transfusion of 500 c.c. of citrated blood was given into the right dorsal metacarpal vein.

The pathologist reported that the tumor was an edematous, degenerating and very hemorrhagic ependymoma. The concentration of protein in the spinal fluid was 9,000 mg. per 100 c.c. below the tumor and 360 mg. above the tumor.

Course. The patient's convalescence was uneventful and he was dismissed on the fourteenth day following operation. Motor power was normal in the lower extremities. There was some paresthesia in the soles of both feet. The left ankle jerk was absent.

Case 2. In 1938, a white woman, twenty-one years of age, registered at the clinic seeking relief from backache and sciatic pain of three years' duration. She stated that when diving three years before she had strained her back and had felt something give way, but that she had not had pain until the next day. During the subsequent days she had experienced rather severe aching pain in the lumbosacral region. The pain was more severe at night than in the daytime and was aggravated by coughing and sneezing. The pain had been present almost every day since it had begun. About nine months after the onset of the backache left sciatic pain had developed and had been so severe that she had been bedfast for a considerable period. Later the pain had involved the region of distribution of the right sciatic nerve also. After the pain had become bilateral, straining at stool also had become painful.

Examination. Findings at general examination were within normal limits. On orthopedic examination, the back was flat, the normal lordosis was absent, and some slight dorsolumbar curvature was present. Motions of the back were markedly limited. There was tenderness over the lumbosacral region and straight leg raising was markedly limited on both sides. The lumbar portion of the spinal column and pelvis were normal to roentgenologic examination.

The right patellar reflex was markedly diminished, both Achilles reflexes were absent, the right internal hamstring reflex was markedly diminished, the right external hamstring reflex was absent, and the left external hamstring reflex was diminished. There was tenderness along the course of the left sciatic nerve. Results of laboratory tests were within normal limits.

A presumptive diagnosis of protruded intervertebral disk was made by an orthopedist, a neurologist, and a neurosurgeon, and visualization of the spinal canal with the aid of air (spinogram) was advised as a preliminary to laminectomy. On the roentgenographic table, a spinal puncture needle was introduced into the first lumbar interspace. This was done for diagnostic purposes and as a step in making the spinogram. Fluid was not obtained but terrific pain was produced in the legs. A spinal puncture needle was then introduced in the second lumbar interspace, with similar findings. Another needle was introduced in the third lumbar interspace and xanthochromic fluid (+4) was obtained under a pressure of 10 cm. When the jugular veins were compressed, the pressure rose to 18 cm. but the patient became extremely rigid and cried with terrific pain in both legs. The pressure promptly fell to 10 cm. and, after 4 c.c. of fluid had escaped, the pressure was zero; in fact, no more fluid could be obtained. Then, injecting small fractions, about 2 c.c. of air at a time, it was possible to obtain in all about 20 c.c. of xanthochromic fluid which congealed on standing. With the injection of each small fraction of air, the patient likewise cried with terrific pain in her legs.

Operation. Immediate operation was performed and a large ependymoma was uncovered and removed completely (Fig. 7). The tumor filled the spinal canal and had destroyed a good portion of the filum terminale. In addition it had involved the tip of the conus medullaris. It

extended to the lower border of the second lumbar vertebra. It was necessary to resect a portion of the conus medullaris to effect complete removal of the tumor.

Later, the spinal fluid which had been removed at the time of making the spinogram was reported to contain approximately 8,000 mg. of protein per 100 c.c.

Course. Convalescence was uneventful. The postoperative neurologic examination disclosed normal patellar reflexes with complete absence of both Achilles reflexes.

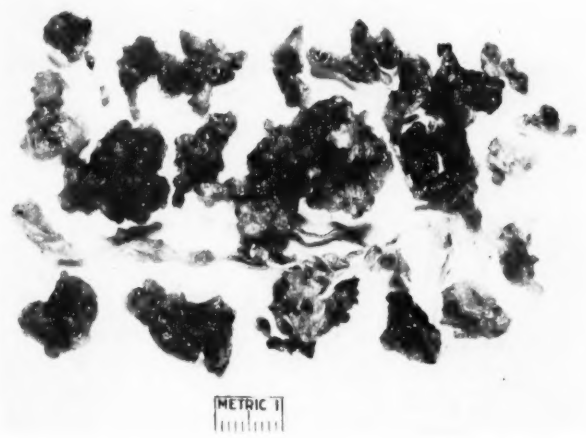


FIG. 7. Ependymoma of filum terminale that was removed piecemeal from patient described in Case 2. Three years later, an examination, including a spinogram, preliminary to marriage, revealed no evidence of recurrence and the patient was free of pain.

In this case, the features which suggested protruded intervertebral disk were (1) the history of trauma, (2) the backache and, later, the unilateral and then bilateral sciatic pain. Suggesting neoplasm were (1) the almost complete lack of freedom from pain at any time and (2) the bilaterality of the sciatic pain. The presence of neoplasm was confirmed by the findings of (1) yellow fluid and (2) the block without paralysis.

Case 3. A man, fifty-three years of age, was referred to the clinic for intraspinal exploration, because, at the time he had been operated on elsewhere for a protruded intervertebral disk, a tumor of the spinal cord had been found and had been only partially removed. Compensation was involved in this case.

The history obtained from the patient was that six years before his admission to the clinic he had fallen twenty feet, after which he had suffered from pain low in the back and in the left buttock. The pain also would extend down the back of the left thigh to the knee. This pain had been aggravated by coughing and sneezing. About two and one-half years before we saw the patient, laminectomy had been performed and a "hypertrophied ligamentum flavum and a slow growing tumor were excised." After this the patient had been free of pain and able to work for amost two years. Then, he had fallen four feet in the sitting position and immediately had experienced severe pain low in the back. He had worked one and one-half days but then had been obliged to give up his work on account of pain.

At the time the patient came to us he was complaining of pain low in his back and in

both thighs. The pain in the left thigh was greater than that in the right; it was increased by coughing, sneezing and straining.

An orthopedic surgeon saw some roentgenographic evidence of spondylitis, with lipping of the vertebrae, but not of such a degree as to require orthopedic treatment.

Examination. There was marked limitation of all spinal motions and marked diminution of the left patellar reflex. The Lasègue sign was bilaterally positive. On lumbar puncture a complete subarachnoid block was revealed and yellow fluid containing 600 mg. of protein per 100 c.c. was obtained. A spinogram revealed residual lipiodol in the spinal canal and air obstructed at the site of a previous laminectomy which had included the first and second lumbar vertebrae.

Operation. This consisted of extension of the previous laminectomy, with complete removal of a neurofibroma which arose from the first lumbar sensory root on the left. The tumor was so large it was necessary to extend the laminectomy more widely than usual to the left, in order to extricate the tumor from beneath the lower end of the conus medullaris and the upper part of the cauda equina.

Course. Convalescence was uneventful. Postoperative neurologic examination revealed the left patellar reflex still decreased and, in addition, the left Achilles reflex was diminished. There was anesthesia in the dermatome supplied by the left first lumbar nerve.

Evidence for protruded intervertebral disk consisted in (1) the history of trauma, (2) the unilateral sciatic pain and (3) the unilateral neurologic signs. The evidence for tumor included (1) the fact that the lesion was higher than most protruded intervertebral disks, (2) the history of a tumor having been found at examination elsewhere, (3) the yellow cerebrospinal fluid and (4) the complete block without paralysis.

Since this paper is dealing principally with spinal cord tumors that have given symptoms and signs suggestive of protruded intervertebral disk, naturally the question arises whether or not protruded intervertebral disks might produce the symptoms and signs suggestive of spinal cord tumor. Large protrusions of intervertebral disks do at times produce all the symptoms and signs that would have led to a diagnosis of intraspinal neoplasm prior to establishment of the syndrome of protruded intervertebral disk. The following case is of this type.

Case 4. A woman, thirty-eight years of age, came to the clinic with a chief complaint of pain in her legs of five months' duration. In 1933, or ten years before her registration, she had undergone tonsillectomy and several diseased teeth had been extracted because of low backache and soreness in the posterior part of the left thigh. The pain had been relieved following the operations. Six years later, she again had complained of low backache and examination elsewhere had resulted in a diagnosis of "congenital back" and she had been advised that she would have to get used to living with it. She had worn a corset with a sacro-iliac support and her symptoms had been relieved. Since that time, she had had recurrent attacks of backache. The backache had been precipitated by colds, menstruation, straining, long trips and bowling. In May, 1943, six months before her registration, she had noticed gradual, although relatively rapid, onset of aching pain from the gluteal region to the left ankle. The pain had been less when she was resting in bed, in the dorsal recumbent position, than when she was up and about. She also had noticed extension of the pain to both gluteal regions and tingling sensations in her left foot and leg. Coughing and sneezing would aggravate the pain when it was present or cause it to begin when it was not present. In the three weeks before we saw the patient she had noticed similar, although much milder, symptoms in her right leg. Motion of the head also had aggravated the pain in the legs. There was no history of trauma to the back.

Examination. General physical examination did not disclose anything abnormal. Examination of the back revealed that all spinal motions were markedly decreased and very painful. Bending forward would result in a list of the trunk to the left. Sensation was intact and there was no atrophy of the muscles. Both ankle jerks were absent. There was a positive Lasègue sign on the left side and tenderness along the course of both sciatic nerves. Roentgenologic examination of the back revealed some narrowing of the lumbosacral interspace and also of the space between the fourth and fifth lumbar vertebrae. Lumbar puncture was performed in the second lumbar interspace. The fluid was clear. There was no evidence of subarachnoid block on Queckenstedt test. The fluid in the lumbar canal was replaced with air (spinogram) and roentgenograms were made (Fig. 2). These films revealed a block of the subarachnoid space at the fourth lumbar interspace and there was no air below the level of the fourth intervertebral disk. The total protein content of the spinal fluid was 80 mg. per 100 c.c. A diagnosis of intraspinal lesion, with the weight of opinion 90 per cent for protruded intervertebral disk and 10 per cent for neoplasm, was made and surgical removal was advised.

Operation. On November 16, a huge protrusion of the fourth lumbar disk, which blocked the spinal canal, was removed through a partial laminectomy wound. There was no evidence of a spinal cord tumor.

The main findings which led to a diagnosis of protruded intervertebral disk rather than of spinal cord tumor were the long history of recurrent bouts of low back and sciatic pain, the fact that the pain had remained unilateral until shortly before we saw the patient, that although there was a complete subarachnoid block the total protein content of the spinal fluid was only 80 mg. per 100 c.c. immediately above the obstruction, and that the neurologic findings were limited to diminution of the Achilles reflexes bilaterally.

ANALYSIS OF TWENTY-SIX CASES IN WHICH INTRASPINAL TUMORS MASQUERADED AS PROTRUDED INTERVERTEBRAL DISKS

It is generally conceded that although protruded disks do occur in women they are more frequently seen in men. This is probably due to the fact that men more often subject their backs to unusual stress and strain. Since these factors of stress and strain are not ordinarily considered important in cases of tumor, it would be expected that tumors would occur with about equal frequency in the two sexes. In the group of cases of tumor analyzed, twelve of the patients were females and fourteen were males, 46.2 per cent and 53.8 per cent respectively. Concerning protruded intervertebral disks, an analysis by Walsh and me revealed that 28.8 per cent of the patients were women and 72.5 per cent were men.

The average age of patients at operation for protruded disk was 42 years and, for this group of tumors, 42.8 years. It has been fairly well established that protrusions of intervertebral disks are the result of trauma to the spinal column. It is likewise generally accepted that trauma does not produce tumors of the spinal cord. Yet in this group of cases of tumor, there was a history of trauma preceding the onset of symptoms in 42.4 per cent of the cases.

Neurologic surgeons are accustomed to seeing patients who give long histories of recurring low back or sciatic pain, or of both types of pain, and

who finally receive a diagnosis of, and are operated on for, protruded intervertebral disks. It was rather surprising to learn that 84.6 per cent, or twenty-two, of the twenty-six patients with tumor had given histories of

TABLE 1

Intraspinal tumors masquerading as protruded intervertebral disks.

	Tumor	Protruded intervertebral disk*
Males, per cent	53.8	72.5
Females, per cent	46.2	28.8
Age at operation, years	42.8	42
History of trauma, per cent	42.4	55
Symptoms intermittent, per cent	84.6	86

* For comparison.

intermittent pain. The history of intermittent pain is elicited in only 86 per cent of cases of protruded intervertebral disk (Table 1). The average duration of symptoms in the group of twenty-six cases of tumor was 6.26 years. One patient with an ependymoma of the filum terminale had intermittent pain for twenty-three years before coming to operation. A man of seventy-three years had complained of recurring backache for forty years and, when he was operated on for a protruded intervertebral disk, a myeloma at the lumbosacral space was encountered in spite of the fact that roentgenologically the bones revealed no evidence of a neoplasm. The shortest duration of symptoms before operation was five months in the twenty-six cases of tumor.

For many years it has been taught that persistent bilateral sciatic pain should be considered to be due to an intraspinal tumor until proved otherwise. In this group of twenty-six cases, ten of the patients complained of

TABLE 2

Intraspinal tumors masquerading as protruded intervertebral disks.

Situation of pain	Cases	Per cent
Low back *and* sciatic pain	20	76.9
Low back pain *without* sciatic extension	5	19.2
Sciatic pain *without* backache	1	3.8

Average duration of symptoms prior to operation, 6.26 years

Sciatic pain	Cases	Per cent of 26 cases (see above)	Protruded intervertebral disks, per cent*
Bilateral	10	38.5	15
Unilateral	11	42.3	75

* For comparison, based on 500 cases.

bilateral sciatic pain; yet eleven patients had pain in only one lower extremity and, what is even more interesting and important, is the fact that five of the patients had backache only, in spite of the fact that they came to operation for relief of incapacitating symptoms and, in each case, an intraspinal neoplasm involving the cauda equina was found and removed. These five cases, it seems to me, are excellent evidence of the value of diagnostic lumbar puncture and also of the fact that, clinically and neurologically, at times it is impossible to make accurate diagnosis of, and to localize, an intraspinal lesion until a lumbar puncture, with or without visualization of the spinal canal, has been performed (Table 2; Fig. 8).

Tumors of the spinal cord will, if left long enough, produce neurologic signs that lead to their diagnosis and usually their localization. However, it does not seem to be good practice of medicine to allow the patient to suffer pain and the danger of irreparable damage to the spinal cord while awaiting a diagnosis and surgical removal of the tumor. One must, therefore, resort to diagnostic lumbar puncture, to determination of total protein in the cerebrospinal fluid and, possibly, to myelography in cases of root pain in which neurologic signs are scanty or absent.

In this group of twenty-six cases of intraspinal tumor only one patient had paraplegia, with a sensory level discernible. In ten cases, the ankle jerks were diminished or absent and in five, abnormalities of the patellar reflex were found. One patient had bilateral foot drop. Neurologic examination of the other nine patients gave essentially negative results (Table 3).

FIG. 8. Two neurofibromas on one nerve root, that were removed from the spinal canal opposite the second lumbar vertebra in the case of a woman fifty-seven years of age who came to the clinic complaining of intermittent low back and left sciatic pain of six years' duration. Her left ankle jerk was absent and she had hypalgesia in the first sacral dermatome. If a spinogram had not revealed the two tumors, she would have been operated on for protrusion of the lumbosacral disk.

TABLE 3

Intraspinal tumors masquerading as protruded intervertebral disks: neurologic findings.

Finding	Cases	Totals
Paraplegia, sensory level discernible	1*	
Ankle jerk diminished or absent	10	17
Knee jerk diminished or absent	5	
Foot drop (bilateral)	1	
Neurologically negative	9	9
Totals	26	26

* Meningioma T-10; multiple disks.

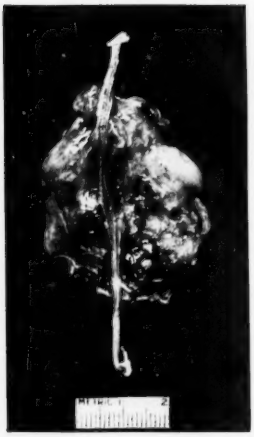


FIG. 9. An ependymoma, which took its origin from the intradural portion of the filum terminale, removed from a patient who came to the clinic because of severe low back and bilateral sciatic pain. The patient's symptoms had their onset following injury and he had been treated elsewhere for meningitis. In addition to this tumor, the patient had a marked degree of spondylolisthesis. The patient was fourteen years of age. The presence of a tumor was recognized when yellow fluid was obtained on lumbar puncture, and the tumor was localized by differential spinal punctures. It extended from the second to the fifth lumbar vertebrae inclusive.

It is known that in the presence of ependymomas of the filum terminale, the concentration of total protein in the cerebrospinal fluid tends to be high and, with this knowledge, on several occasions I have been able to make a preoperative diagnosis of ependymoma of the filum terminale after seeing the fluid, or the report on it, in cases in which patients have been sent for lumbar puncture with a provisional diagnosis of protruded intervertebral disk[2] (Fig. 9). The average reading for total protein in nine of these cases of ependymoma was 3,355.5 mg. per 100 c.c., whereas the average concentration in the fluid of twelve patients who had neurofibromas was 700 mg. (Table 4). The fluid removed from the spinal canal below an ependymoma is usually dark yellow and often clots after being exposed to the air. This sometimes happens to the fluid immediately above the tumor but the fluid above the tumor is likely to be less concentrated than that below, and this fact is important in localizing tumors by multiple or differential puncture (see Case 1).

CONTRAST MYELOGRAPHY AND DIFFERENTIAL SPINAL PUNCTURE

Although the spinogram is not as reliable in diagnosis and localization of intraspinal space-taking lesions as are radiopaque myelograms, the spinogram will suffice in most instances if it is used as it should be used (Table 5); that is, if it is employed as a laboratory procedure, to be considered in the light of (1) the history, (2) the general, orthopedic, and neurologic examinations, (3) the appearance of the spinal column in ordinary roentgenograms, (4) the analysis of the findings on lumbar puncture and (5) examination of the cerebrospinal fluid. If there

TABLE 4

Intraspinal tumors masquerading as protruded intervertebral disks.
Total protein in cerebrospinal fluid.

Highest 9,000 mg. per 100 c.c.		Lowest 40 mg. per 100 c.c.		Average 1483 mg. per 100 c.c.
Ependymomas	9 cases →	Average →		3,355.5 mg. per 100 c.c.
Neurofibromas	12 cases →	Average →		700.0 mg. per 100 c.c.
Meningiomas	2 cases →	40 mg.	and	440.0 mg.

Of 265 cases of protrusion of lumbar intervertebral disks, the total protein was less than 40 mg. per 100 c.c. in 34 per cent. The value for total protein in cases of protruded intervertebral disk is rarely more than 100 mg. per 100 c.c.

is a complete subarachnoid block, the spinogram will usually give a good outline of the mass which is blocking the subarachnoid space, particularly if it is in the lumbar portion of the spinal canal. For nonobstructing lesions above the conus medullaris, myelography with gas has been unsatisfactory in our hands at the clinic. Lipiodol or pantopaque, which are radiopaque and can be visualized with the roentgenoscope, are then employed in diagnosis and localization of the lesion.

For localization of neoplasms below the conus medullaris, in cases in which spinograms have not been made for one reason or another, or in which the spinogram is unsatisfactory, differential or multiple spinal punctures are indicated (see Case 1). I feel that it is unwise to inject a nonabsorbable radiopaque substance in the presence of a high concentration of

TABLE 5

*Intraspinal tumors masquerading as protruded intervertebral disks. The use of contrast myelography**

	Cases	Positive	Inconclusive
Spinogram (air myelogram)	15	12	3
Radiopaque oil (lipiodol)	6	6	
Differential spinal puncture†	3	3	
Routine lumbar puncture (only)	4		

* In some cases more than one procedure was employed; for example, spinogram and roentgenogram after injection of lipiodol.

† Radiopaque substances should be used with caution in presence of high total protein in the cerebrospinal fluid.

protein in the cerebrospinal fluid. The tumors with which neurosurgeons are particularly concerned in the differential diagnosis of protruded intervertebral disks often are associated with high total protein. If there is, in addition, a subarachnoid block the tumor can be accurately localized between two spinal puncture needles. In the absence of complete block, the neoplasm usually can be localized accurately by comparing a specimen of fluid from below the suspected level with a specimen from above. Of course, to do this one must take into consideration all the other available information concerning the patient.

SURGICAL TREATMENT

Once the diagnosis of a space-taking intraspinal lesion has been made and removal of that lesion has been decided on, the surgeon should be equipped adequately to care for any exigency. If the lesion is an extradural protrusion of an intervertebral disk, and the level of the protrusion is known, the operative procedure should be of relatively short duration and should necessitate the sacrifice of little or no bone of the spinal column. Exceptionally, the operation for removal of a protruded intervertebral disk may be time consuming, difficult and require complete laminectomy. An electrosurgical unit and a suction apparatus are considered essential parts of the

surgical equipment. In cases of unilateral pain, unilateral reflection of the erector spinae muscles from the spinous processes and laminae at the site of protrusion is adequate to permit unilateral resection of the ligamentum flavum and exploration of the nerve root and disk. In about 85 per cent of cases, the fragmented and protruded portion of the disk can be removed without sacrifice of any bone[1] (Fig. 10). In the rest of the cases some bone—a few bites from the margin of the lamina or the entire lamina—may be removed necessarily to obtain adequate exposure.

It is my practice to remove any fragments of cartilage that lie free in the spinal canal, any fragments projecting into the spinal canal and those

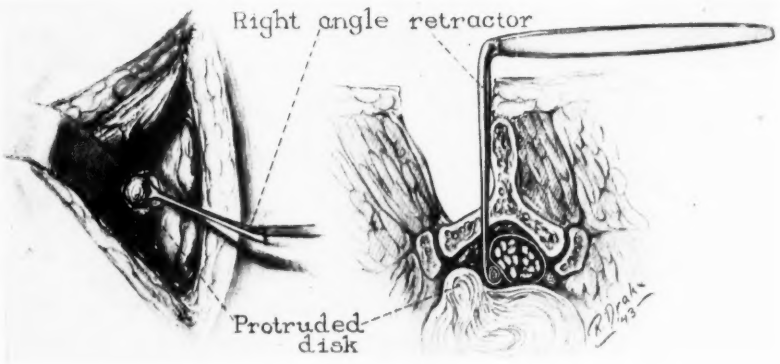


FIG. 10. Extent of the operative procedure which is required in the average case of protruded intervertebral disk. A special right-angled retractor is in place, retracting the edematous, compressed nerve root and exposing the protruded disk which is to be removed with a modification of the Gruenwald forceps.

loose fragments that lie in the intervertebral space. No attempt is made to curet the space or to remove the entire disk. The use of sharp cutting instruments in the intervertebral space is fraught with real danger. I have seen one patient who had an arteriovenous fistula (aorta to inferior vena cava) following removal elsewhere of a protruded intervertebral disk. I have been told of another patient who went into a state of shock and died following removal of a protruded intervertebral disk. When postmortem examination was made, a perforation of the abdominal aorta, with fatal hemorrhage, was discovered.

Removal of intraspinal neoplasms requires the sacrifice of one or more laminae, and usually (except in the cervical region of the spinal column) one or more spinous processes and both laminae of one or more vertebrae are removed. It is essential in removing tumors of the spinal cord to have adequate exposure in order to permit complete removal of the tumor and accurate hemostasis. In the case of neurofibromas it is necessary to expose the involved nerve root above and below the tumor so that the entire tumor

can be removed and thus recurrence can be avoided. In removing meningiomas it is necessary to resect the meninges widely around the neoplasms to forestall recurrence. The dura mater adjoining the tumor is usually richly supplied with newly formed blood vessels and meticulous attention to hemostasis must be given lest a postoperative clot develop and mar what otherwise would be an uneventful convalescence. In the case of ependymomas arising from the filum terminale and producing low back or sciatic pain, or both, it is essential to perform laminectomy of sufficient extent (often including the entire lumbar and sacral portions of the spinal column) to permit resection of all involved filum terminale.

In closing laminectomy wounds, hemostasis is next in importance to asepsis. Without the one, paralysis is likely to occur and without the other, death.

If the dura mater has been opened it should be sutured carefully, and it is a valuable aid in securing hemostasis to distend the dural sac with physiologic saline solution at a temperature of 100° F. This distention compresses the extradural vessels and holds the dura mater against the bone; it also diminishes the chance of adhesions developing between the meninges and the spinal cord. The edges of the resected bone should be sealed with bone wax. All extradural bleeding should be controlled by pledgets of muscle, electrocoagulation, silver clips or a plain gauze pack. The bleeding from the muscles is controlled before the bone is removed to expose the spinal canal; sometimes, however, when the self-retaining laminectomy retractor is removed to close the wound, bleeding from the muscles occurs. All bleeding points should be caught and subjected to electrocoagulation. The muscles and fascia should be sutured accurately in layers. The stitches should be tied tightly enough to secure accurate approximation and to prevent bleeding from the surfaces of the muscles but not tight enough to produce ischemia of the muscles, lest they undergo atrophy.

The skin can be closed with interrupted or continuous sutures. Here again it is better to have a little oozing from the skin edges than to have the edges blanched from too tight sewing. Tight stitches in the skin may result in sloughing and delayed healing.

SUMMARY AND COMMENT

In an analysis of the records of twenty-six cases of tumor of the spinal canal, in which symptoms of root pain suggested irritation or compression of the spinal cord or nerve roots by a protruded intervertebral disk, it was found that diagnostic spinal puncture, with or without visualization of the spinal canal, was essential to diagnosis and to localization of the intraspinal lesion.

Of a series of fifteen cases of tumor of the spinal canal, it was found that in eight the symptoms were misleading in that they suggested protruded intervertebral disk. Also, during the period when this series of fifteen patients came to operation, one hundred other patients were subjected to operation for protruded intervertebral disks.

Therefore, in any case of unexplained, intractable, root pain and in almost every case in which protruded intervertebral disk is suspected, diagnostic lumbar puncture should be performed and the protein content of the cerebrospinal fluid should be determined. A value for spinal fluid protein of more than 100 mg. per 100 cc. usually means a neoplasm rather than a protruded intervertebral disk.

One should not await definite neurologic signs before making the diagnosis. The surgical removal of any space-taking intraspinal lesion should be so planned and executed as to cause the minimum of disruption of normal structures and thus restoration of the patient to his usual activities with minimal loss of time will be facilitated.

REFERENCES

1. Love, J. G. Removal of protruded intervertebral disks without laminectomy. *Proc. Mayo Clin.* 1939, *14:* 800.
2. Love, J. G., and Walsh, M. N. Protruded intervertebral disks. *Surg. Gynec. Obstet.*, 1943, *77:* 497–509.

INTELLIGENCE FOLLOWING PREFRONTAL LOBOTOMY IN OBSESSIVE TENSION STATES*

JAMES W. WATTS, M.D., AND WALTER FREEMAN, M.D., PH.D.
Department of Neurology, George Washington University, Washington, D. C.

(Received for publication May 24, 1944)

In 1938, we reported six cases of obsessive tension states following interruption of the frontal association pathways. We have continued our studies on these and similar cases and at the present time can amplify our conclusions based upon forty-five patients studied from six months to seven years after operation.

Prefrontal lobotomy relieves nervous tension and obsessive thinking. Following operation the patient may still cling to the idea that he has tuberculosis or syphilis or that his Eustachian tube is stopped up. A woman may look in the mirror and see just as much hair on her face and arms as before operation when she thought that suicide was the only solution. But if the idea no longer is accompanied by a heavy emotional charge, it loses its importance and no longer dominates the life of the individual.

In the forty-five patients under discussion, it was the emotional charge, therefore, that caused the disability rather than the peculiar ideas themselves. Furthermore, there was no significant deterioration, either intellectual or emotional. Although the average duration of symptoms in these cases was slightly more than ten years, only five patients had been confined to mental hospitals.

If brain-damaging therapeutics are to be employed in patients without mental deterioration, it is important to know how the intelligence is affected by the procedure. If relief of mental pain is secured only by sacrificing the intelligence and understanding, the price is too great.

According to the Encyclopaedia Britannica,[1] "Intelligence or understanding is a term that is still used by psychologists with considerable latitude of meaning. Sometimes it is used as a synonym of 'cognition,' that is to say, it is applied to any of the numerous processes by which knowledge is built up. Sometimes it is restricted to the conceptual process, as distinct from the process of sense perception. Some (psychologists) frankly admit that they do not know and do not care what this 'intelligence' may be which they are measuring, so long as these measurements can be made use of. Lastly, ordinary everyday usage perhaps tends to emphasize the practical character of intelligence as consisting in the ability to employ the right means in order to achieve the various ends pursued."

In this paper, we are concerned with the practical character of intelligence, and if our yardstick is "the ability to employ the right means to achieve the ends pursued," then it would appear that our patients are more intelli-

* Read before The Harvey Cushing Society, New York City, May 17, 1944.

TABLE 1

Symptoms produced by prefrontal lobotomy in 74 cases.
(After Freeman and Watts[3])

Symptom	Total	Persistent	Temporary	Symptom	Total	Persistent	Temporary
Lack of Initiative	73	30	43	Overactivity	22	6	16
Dullness	66	9	57	Witticisms	18	7	11
Disorientation	65	2	63	Startle Reaction	18	7	11
Euphoria	60	22	38	Lack of Distractibility	17	11	6
Apathy	60	6	54	Impulsive Acts	16	9	7
Fatigability	59	14	45	Perseveration	16	3	13
Fluctuation of Attention	58	7	51	Mannerisms	16	—	16
Procrastination	56	29	27	Stupor	16	—	16
Slowness	54	18	36	Decreased Suggestibility	14	12	2
Psychomotor Retardation	54	2	52	Poor Judgment	14	11	3
Lack of Interest	53	5	48	Irritability	14	7	7
Restlessness	53	3	50	Stereotypy	14	2	12
Laziness	52	22	30	Indefatigability	13	10	3
Amnesia	52	1	51	Youthful Appearance	11	10	1
Facetiousness	49	18	31	Aggressiveness	9	4	5
Tactlessness	47	43	4	Elation	9	—	9
Somnolence	45	—	45	Profanity	8	2	6
Blunting	41	3	38	Tantrums	7	2	5
Distractibility	38	10	28	Confabulation	7	1	6
Volubility	30	13	17	Catalepsy	7	—	7
Playfulness	28	8	20	Indecency	6	1	5
Increased Suggestibility	25	16	9	Circumstantiality	5	5	—
Emotional Lability	24	11	13	Delirium	1	—	1
Sarcasm	22	13	9				

gent after lobotomy than before. Before operation only 17 per cent were leading useful lives—13 per cent were employed, 2 per cent were employed part time and 2 per cent were housekeeping. At the present time, 67 per cent are leading useful lives—38 per cent are employed, 11 per cent are employed part time and 18 per cent are housekeeping. This statement does not imply that the patients are restored entirely to normal because many show personality changes indicative of frontal lobe deficit (Table 1), but 67 per cent are now employing their ability in a manner to achieve the ends pursued as compared to 17 per cent prior to operation. Paradoxically then, it might seem that some individuals can function more effectively with less brain in actual operation.

The operative technique has been described and illustrated rather recently, so it need not be discussed here. The accuracy has been improved by adding a guide to the blunt dissector,[5] and the danger of bleeding from the region of the medial longitudinal fissure has been reduced by cutting the white matter near the midline with radial stab incisions.[6]

OBSESSIVE COMPULSIVE STATES

Two patients with disabling compulsive behavior, who have been discussed before,[2,3] are presented here because they have been followed since 1937 and each in a different way illustrates our thesis.

Case 1. Miss M.S., who was 28 years of age at the time of prefrontal lobotomy, had obsessions as a child and had been disabled by them since she was graduated from the University at the age of 20. She had a dread of all kinds of shoes; even dolls' shoes, and white kid shoes were worst of all. She was at the Johns Hopkins Hospital 8 months, after which she was psychoanalyzed. She returned to Puerto Rico where she remained in a sanitarium 2 years and 8 months. While in the sanitarium she received psychotherapy and insulin shock and most of the time she was isolated in her room and did not wear shoes. She allowed nobody to touch her and she was unable to undress before anyone wearing shoes. She arrived in Washington by plane without shoes and when we saw her at her hotel she was barefooted and barelegged.

Prefrontal lobotomy was performed September 21, 1937, but because she was still afraid of contamination, a second, more extensive lobotomy was done 9 days later. She still had all kinds of phobias, but October 20th, a month after operation, she put on stockings and shoes and went out for a walk with her nurse. For some time she wore pumps that she could slip on her feet without touching them with her hands. Although her ideas about shoes persisted, she undertook graduate studies in mathematics at Columbia University and resumed psychoanalysis which continued while she was in New York. After lobotomy she complained of feeling "dumb" and she has been resentful about the lobotomy.

A notice about the patient in a Puerto Rico paper, dated September 20, 1942, reads as follows: "Miss M.S., who graduated Magna Cum Laude at the University of Puerto Rico, has her Master's Degree in Mathematics from Columbia University. She has completed all of her resident requirements for her Doctor's Degree and is teaching courses in Algebra, Trigonometry, and Calculus. Miss S. is working on her Doctor's Thesis now on the subject of 'Mathematics teaching in Puerto Rico'."

Comment. The patient attributes all the progress she has made to psychoanalysis and it is probable that she could not have had the adjustment she has without its assistance. We are not concerned here with trying to evaluate the degree of improvement due to lobotomy and that due to analysis. We merely wish to point out that after an extensive bilateral prefrontal lobotomy, this woman resumed her activities after having been disabled for eight years, and demonstrated a high degree of intelligence in the pursuit of her graduate studies.

Case 2. Mr. H.D., a teacher and tool-designer aged 54, was neurotic all of his life, and complained of a peculiar clicking in the ear and of pressure in his head that made it impossible for him to continue work. For a year and a half his only task was to run errands for his wife. He suffered from nervous tension, anxiety, fear of going insane, depression of spirits and an exhausted feeling. At about the age of 40, he began experiencing twitching of the facial muscles, with actual subluxation of the jaw which was also associated with marked blocking and difficulty in speech, grimacing, and obsessive hair-pulling. The patient was intelligent, had marked mechanical aptitudes and no demonstrable physical or neurologic disturbances.

Prefrontal lobotomy was carried out on May 12, 1937, with immediate replacement of the nervous tension by a rather vacuous euphoria. Rather slow resumption of his activities followed, without recurrence of the mannerisms.

In talking about his symptoms a year after lobotomy he stated: "The feeling in the ear is still there. It is not so intense, and it does not occupy my attention continuously. Before operation, I was conscious of it all day, every hour, every minute. As Professor William James of Harvard said, it used to be in the focus of my attention. Now it has moved out to the margin. Before it occupied my attention to the exclusion of all else. I couldn't concentrate on anything. Now I think of it once in awhile but it doesn't worry me. I can concentrate on other problems." Referring to a machine he had invented since operation he said: "I have had this new machine in mind for a good many years, even before stopping work as a tool designer, but I couldn't get it clear. It seemed at first that parts would have to be so delicate that ma-

terial of the proper strength could not be found to produce the instrument. During the past few months it came to me clearly and I sat down and drew it. I not only think it will work, I know it will work." The drawing was carefully made, neat and showed no evidence of carelessness.

Toward the end of the summer he wrote as follows: "The patent is coming along fine. Six of the nine claims have already been rated as allowable. It is difficult to market now owing to business conditions. I, myself, am following Doctor Lindlahr's theory that heat trouble comes from inside instead of outside. Plenty of non-heat-producing foods keep me very comfortable. I am enjoying the theory of the Christian Scientists and the Spiritualists that mental attitude is everything. This has been the most enjoyable summer I have ever had—."

Five months later he reported by letter: "You will probably be pleased to learn that I am a working man again after nearly seven years out of the drafting room. I am not nearly so nervous in making ink drawings on linen as I used to be."

In July 1943, he reported that he is still employed in the same position, working 54 hours a week. He had just completed the design of a rather intricate machine which would cost several thousand dollars to make.

Comment. Having been freed of nervous tension, this man turned his attention from his Eustachian tube to tool designing, in which he is employing his abilities, not only with energy but also imagination. The cutting off of his ideas concerning himself has favored a change from a destructive imagination to a constructive imagination.

TENSION STATES

There are other patients who are obviously under nervous tension who have no compulsions and no complaints about any part of the body. Some are disabled by a feeling of inferiority or insecurity or inability to make a decision. Others, while still working, do so only at a tremendous expenditure of effort, and the margin between ambition and accomplishment is so great that suicide seems to offer the only solution.

The difficulties some patients have making decisions is illustrated by a man of 26, who wrote as follows:

"There is such a vast *mass* of material to be *examined*, and it is often so *devious*, *subtle*, and *elusive*, in its nature, and, moreover, there are so many *variables* to give due and adequate *consideration* to that I often, (or at least *sometimes*), find myself involved in a sufficiently perplexing preponderance of *seemingly* paradoxical problems to prevent successful and efficient and logical solution and answer to the problem of decision."

A prefrontal lobotomy was performed April 1, 1942. Soon after operation he was very slow, but once he started something, continued indefinitely. On one occasion he shaved with an electric razor for five hours.

About six months after lobotomy, he became very active, rolled the lawn, cut the grass, and cleaned out brush around the brook. One day he started work at 7 a.m., and 8 a.m., when told breakfast was ready, he replied that he was busy. At noon, his wife called him to come to lunch, and he told her to leave him alone, that he was busy. When she insisted at 5 p.m. that he come in to eat, he became very much annoyed and tore off her dress. When seen March 16, 1943, all his indecision had disappeared.

In January 1944 he reported that he had a job as a janitor in a school with a salary of $32.00 a week, the first money he had ever earned. He still went into detail about everything, about his trip, his job, etc., but he did not deviate from the main line of thought as he used to. The patient still wanted to finish high school which he had to stop at the end of the second year. His ambition is to be a psychiatrist, a teacher or a university president.

Comment. For the time being, this man is willing to earn a living in a more modest position, while taking a high school correspondence course. It is too soon to say whether he will be content with a routine job as a laborer or whether he will be able to achieve something in a more intellectual sphere.

Other patients with tension states know something is wrong but can't put their finger on their trouble. They want to be relieved, but don't know just what they want to be relieved of. This is illustrated by the following case.

A lawyer, 35 years of age, developed nervous symptoms in the Spring of 1938. At that time he was a partner in a law firm in New York. His work deteriorated so much that in December 1938 he was dropped from the firm.

When asked what he was complaining of, he stated that he was unable to find a job. He had tried several times in the past two or three years but could not find anything which paid a salary comparable to that of his old position. Most of the time he sat around home and worried about not being able to find a position. When his wife suggested that he try to find something, he always found some excuse for not doing it. He had become irritable, slept poorly, and sat around all day worrying about not having anything to do. He weighed every question put to him and, when he finally answered, qualified every statement. When asked if he thought that everyone who could not find a position should have a prefrontal lobotomy, he admitted after some consideration that this would be foolish, and yet when asked immediately afterwards why he came to the doctor, he said it was because he could not find a job.

As he was obviously under nervous tension, it was decided to give him the benefit of a prefrontal lobotomy; so on November 7, 1940, he was operated upon. This man did not return to work until April 1941, but he no longer worried about being out of work. In April he opened his office for the practice of law, but after six months closed it because he had no clients. In January 1942, at our suggestion, he got a clerical position with the Government, and discharged his duties satisfactorily. He is now employed as examiner for one of the Government Boards.

Individuals with obsessive tension states have energy and ambition; they are meticulous, economical and punctual. While they may not always be agreeable, they are good workers and often find that their old positions have been held open for them if they have not been away too long. On returning to work they are usually slow for a while but accurate, and they perform their duties to the satisfaction of the employer. Most of the patients seek work in the same type of employment in which they were engaged before lobotomy. A few may change, like a clerk in the Treasury Department who had never liked anything about his job except getting his pay-check twice a month. Radio had always been his hobby and after operation, still finding the Treasury Department obnoxious, he resigned and became a radio operator.

Patients in this group come to the doctor seeking lobotomy in contrast to those with involutional depressions who are virtually dragged in by their relatives. If they can be freed of nervous tension they believe that they can apply themselves to their tasks and reach their goals. Prefrontal lobotomy relieves nervous tension and often aids the individual in achieving the end he pursues. For those who have set their goal too high, lobotomy brings it closer, but does so by making them more easily satisfied with their accomplishments. It makes them willing to do work commensurate with their abilities.

When the patient and his family ask whether the intelligence is damaged by the operation they are concerned with the practical character of intelligence. In discussing this subject recently Jaeger[4] said, "These people may not be more intelligent after operation, but they can use what they have better than they could before." The ability to resume one's occupation or to earn a living is a good pragmatic test of intelligence. Our observations indicate that in patients disabled by obsessive tension states, the pragmatic intelligence is improved by prefrontal lobotomy.

CONCLUSIONS

1. In forty-five patients with obsessive tension states there was no significant intellectual or emotional deterioration.

2. Disability was not due to the peculiar ideas but to the emotional charge associated with the ideas.

3. Before prefrontal lobotomy 17 per cent were usefully employed and at the present time 67 per cent are leading useful lives.

4. Pragmatic intelligence is improved by prefrontal lobotomy in individuals disabled by obsessive tension states.

REFERENCES

1. Encyclopaedia Britannica. *New York: Encyclopaedia Britannica, Inc.*, 1937, 14th ed., *12:* 457–458.
2. Freeman, W., and Watts, J. W. Some observations on obsessive ruminative tendencies following interruption of the frontal association pathways. *Bull. Los Angeles neurol. Soc.*, 1938, *3:* 51–66.
3. Freeman, W. J., and Watts, J. W. Psychosurgery. Intelligence, emotion and social behavior following prefrontal lobotomy for mental disorders. *Springfield, Ill.: Charles C Thomas*, 1942, 337 pp.
4. Jaeger, R. Discussion of paper by Watts, J. W., and Freeman, W. Proceedings of Philadelphia Neurological Society, March 24, 1944. *Arch. Neurol. Psychiat., Chicago.* (To be published)
5. Watts, J. W., and Freeman, W. Surgical aspects of prefrontal lobotomy. *J. Int. Coll. Surg.*, 1942, *5:* 233–240.
6. Watts, J. W., and Freeman, W. Prefrontal lobotomy: six years' experience. *South. med. J.*, 1943, *36:* 478–486.

NOTICES

THE AMERICAN BOARD OF NEUROLOGICAL SURGERY

The third edition of the *Directory of Medical Specialists* listing names and biographical data of all men certified by the fifteen American Boards is to be published early in 1945. Collection of biographical data of the Diplomates certified since the 1942 edition, and revision of the older listings in that volume are now going forward rapidly. Diplomates are requested to return notices regarding their biographies as promptly as possible after receiving the proper forms from the publication office soon to be mailed to them.

THE ASSOCIATION OF MILITARY SURGEONS OF THE UNITED STATES

The program for the Annual Meeting of the Association of Military Surgeons of the United States to be held at the Pennsylvania Hotel, New York City, November 2 to 4 inclusive, is being rapidly completed. In addition to addresses by the Surgeons General of the Army, Navy, and U. S. Public Health Service and by other distinguished guests, there will be formal papers, panel discussions and scientific and technical exhibits on the latest advances in military medicine.

BASILAR IMPRESSION (PLATYBASIA) A CASE SECONDARY TO ADVANCED PAGET'S DISEASE WITH SEVERE NEUROLOGICAL MANIFESTATIONS. SUCCESSFUL SURGICAL RESULT

HENRY T. WYCIS, M.D.
Department of Neurosurgery, Temple University Hospital, Philadelphia, Pennsylvania

(Received for publication May 13, 1944)

BASILAR impression had been known to the German pathologists for some time. Rokitansky[11] apparently was the first to mention the deformity in 1844. Boogaard,[1] in 1865, described the condition and related its causes and consequences. Virchow[14] submitted more detailed descriptions of the condition in 1876. Grawitz,[4] in 1880, made careful anatomical studies of six skulls with basilar impression. Homén,[5] in 1901, was the first to correlate the neurological abnormalities with the postmortem findings. He demonstrated the local pressure effects of the odontoid process on the medulla oblongata.

It was not until 1911 that the condition was recognized as a clinical entity. At this time Schüller[12] made the first premortem diagnosis, describing the effects of the bony deformity on the central nervous system. Since that time, clinico-pathologic reports have appeared by Sinz,[13] Kecht,[7] Krause,[8] Juhlin-Dannfelt,[6] Merio and Risak,[10] and Ebenius.[3]

In 1939, Chamberlain[2] described four cases of basilar impression with bizarre neurological abnormalities. In two cases, suboccipital decompression, carried out by Dr. Temple Fay, resulted in improvement. Chamberlain's report is important in that it stimulated a growing interest in this condition in this country. The excellent report by List[9] on the neurological changes associated with developmental anomalies of the occipital bone, atlas and axis, further elucidated the problem.

From the standpoint of etiology basilar impression may be "primary" (result of a congenital, developmental anomaly) or "secondary" (result of bony softening and moulding). Trauma may be an aggravating feature in any case but is believed never to be the underlying cause of the disease. Rickets, osteomalacia, hyperparathyroidism and osteitis deformans (Paget's disease) have been listed as causes, in many instances without convincing proof. Walsh, Camp and Craig,[15] in reporting a successful surgical result, list Paget's disease as a cause of secondary basilar impression but do not cite specific examples.

A case is here reported, for the first time, of basilar impression secondary to Paget's disease producing severe neurological manifestations. The patient was treated successfully by high cervical laminectomy combined with suboccipital decompression.

CASE REPORT

Mr. R. K., aged 50, was admitted to the Neurosurgical Service of Temple University Hospital, January 11, 1944. He complained of severe bilateral occipital neuralgia, bilateral loss of hearing, weakness of the right arm and leg with dragging of the latter extremity, numbness of the right forearm and foreleg, difficulty in speech with regurgitation of fluids through the nose, and wobbling gait.

He stated that he was entirely well until five years before admission when his brother-in-law suddenly pulled his head in a tussling match. He experienced sudden pain at the back of his head which radiated to the vertex. At first this pain would come in paroxysms but for the last year it had been almost continuous. Loss of hearing had been bilateral and progressive, existing for a number of years, the right ear being involved more than the left. Approximately one year before admission there was onset of progressive weakness of the right arm and leg so that, on admission, he had to drag the right leg in attempting to walk. Simultaneously there was noted a feeling of numbness, starting in the region of the right elbow and progressing to the fingers, and also starting in the region of the right knee and progressing to the toes. He likewise complained of numbness of the four fingers of the left hand. The right foot always felt cold. During this year his gait had become quite unsteady. For the last few weeks his speech had been thickened and indistinct and he noted, on occasions, that fluids would regurgitate through the nose on attempted swallowing. Vision was impaired in the right eye, which he attributed to an ocular injury sustained many years ago. During the last four years the head had steadily increased in size. He had been accustomed to wearing a hat sized $6\frac{7}{8}$; on admission it was $8\frac{1}{4}$. There had been a 33-lb. loss in weight in the last few months.

At the age of 11 he fell from a tree and fractured his coccyx. Herniorrhaphy was performed in 1929.

Examination. The general appearance in the advanced stage of Paget's disease was striking. The short, squat figure with bent shoulders, sunken chest, curved back, and great head hanging forward, wobbling along, was a true living justification of Sir James Paget's description of the disease in 1876. The great flattened head seemed to "mushroom" on top of the cervical spine. The veins and arteries of the temporal areas were unduly prominent. The movements of the head were limited in all directions but particularly in the lateral deviations to the shoulders. Palpation showed marked atrophy of the posterior cervical group of muscles. The spinous processes appeared thickened and prominent. The pupils were equal, but light reaction was sluggish in the right eye due to the presence of a corneal scar. The light reflex in the left eye was normal. Vision was impaired in the right eye only. The visual fields were grossly normal. The fundi appeared normal. The external ocular movements were normal in all fields of movement but there was a horizontal nystagmus of second degree on either lateral gaze. The corneal reflexes were normal and there did not appear to be any sensory abnormalities in any of the trigeminal fields. The facial expressional movements were equal. There was bilateral eighth nerve deafness, more pronounced on the right side. The gag reflex was present on both sides and the uvula and soft palate moved in the midline. The left shoulder was slightly lower than the right. The tongue protruded in the midline without tremor or atrophy. The speech, nevertheless, was quite thickened and almost indistinct. There was difficulty in swallowing fluids and, on occasion, the fluid would regurgitate through the nose.

The gait was markedly ataxic with falling to either side in the Romberg position. In attempting to walk, he would drag his right lower limb. The deep tendon reflexes were bilaterally exaggerated, but more so on the right side. There was a Hoffmann sign on the right side with bilateral Babinski responses, more easily elicited on the right side. There was marked weakness in motor power of the right upper and lower limbs. The motor weakness was mild on the left side. There was a bilateral dysmetria and dyskinesia of the upper limbs, more pronounced on the right side. Ataxia was pronounced in both lower limbs, but also was more exaggerated on the right side.

Sensory disturbances to pain and temperature were not distinct. However, he was able to appreciate an ice tube more acutely on the entire left side with a definite increase in sensa-

tion bilaterally at the level of the second cervical dermatomere. Vibration, position and stereognostic sense were unimpaired.

Laboratory Studies. The urinalysis and complete blood counts were normal. The spinal fluid and blood serology were normal. The blood calcium was 10.2 mgm. per 100 cc.; the blood phosphorus was 4.5 mgm. per 100 cc. while the alkaline phosphatase was elevated to 36 Bodansky units per 100 cc.

Roentgenograms. I am indebted to Dr. W. Edward Chamberlain for the following comments and descriptions of the roentgenologic findings in this case.

"Advanced Paget's disease of the skull and upper cervical spine is here visualized (Fig. 1). This is characterized by thickening of the bone with loss of demarcation of the outer table of the skull. Many small distinct and conglomerate areas of increased bone density are seen. These are characteristic of the disease.

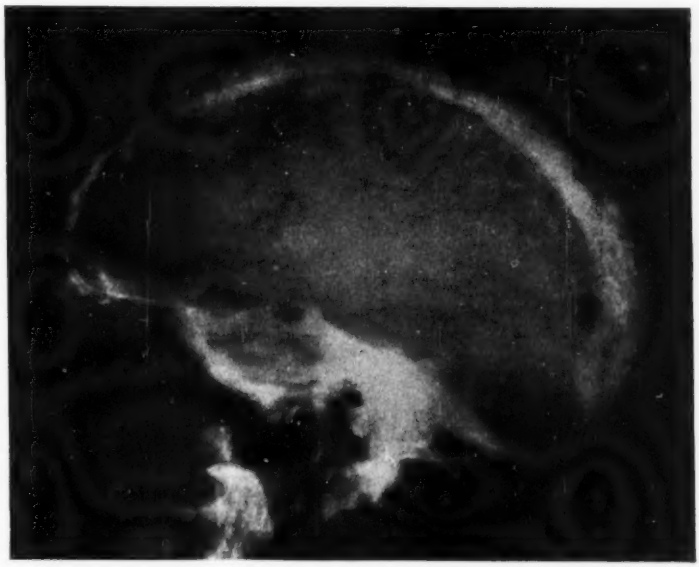


FIG. 1. Right lateral projection of skull showing advanced Paget's disease with secondary platybasia (marked flattening of the "basal angle" between floor of anterior fossa and clivus) and basilar impression (invagination of occipital condyles, margins of foramen magnum and other basal structures into the brain space). In Paget's disease the bones become softened, even when their mineral content is high. The deformities here visualized are a result of that softening.

"Paget's disease produces marked softening of the bone, even in the presence of increased bone density (increased calcium content). As a result of this softening a marked degree of secondary basilar impression has developed. The cephalo-caudal dimension of the cranium is at least 2 cm. less than the normal. The angle between the floor of the anterior fossa and the clivus, normally of the order of 135 degrees, has flattened to approximately 160 degrees. The basilar invagination is most marked at the ventral margin of the foramen magnum, less marked at its dorsal margin. As a result of this, the plane of the foramen magnum is inclined dorsad and obviously there must be a kinking of the brain stem where it passes around the invaginated odontoid process and the ventral margin of the foramen magnum.

CASE REPORT

Mr. R. K., aged 50, was admitted to the Neurosurgical Service of Temple University Hospital, January 11, 1944. He complained of severe bilateral occipital neuralgia, bilateral loss of hearing, weakness of the right arm and leg with dragging of the latter extremity, numbness of the right forearm and foreleg, difficulty in speech with regurgitation of fluids through the nose, and wobbling gait.

He stated that he was entirely well until five years before admission when his brother-in-law suddenly pulled his head in a tussling match. He experienced sudden pain at the back of his head which radiated to the vertex. At first this pain would come in paroxysms but for the last year it had been almost continuous. Loss of hearing had been bilateral and progressive, existing for a number of years, the right ear being involved more than the left. Approximately one year before admission there was onset of progressive weakness of the right arm and leg so that, on admission, he had to drag the right leg in attempting to walk. Simultaneously there was noted a feeling of numbness, starting in the region of the right elbow and progressing to the fingers, and also starting in the region of the right knee and progressing to the toes. He likewise complained of numbness of the four fingers of the left hand. The right foot always felt cold. During this year his gait had become quite unsteady. For the last few weeks his speech had been thickened and indistinct and he noted, on occasions, that fluids would regurgitate through the nose on attempted swallowing. Vision was impaired in the right eye, which he attributed to an ocular injury sustained many years ago. During the last four years the head had steadily increased in size. He had been accustomed to wearing a hat sized $6\frac{7}{8}$; on admission it was $8\frac{1}{4}$. There had been a 33-lb. loss in weight in the last few months.

At the age of 11 he fell from a tree and fractured his coccyx. Herniorrhaphy was performed in 1929.

Examination. The general appearance in the advanced stage of Paget's disease was striking. The short, squat figure with bent shoulders, sunken chest, curved back, and great head hanging forward, wobbling along, was a true living justification of Sir James Paget's description of the disease in 1876. The great flattened head seemed to "mushroom" on top of the cervical spine. The veins and arteries of the temporal areas were unduly prominent. The movements of the head were limited in all directions but particularly in the lateral deviations to the shoulders. Palpation showed marked atrophy of the posterior cervical group of muscles. The spinous processes appeared thickened and prominent. The pupils were equal, but light reaction was sluggish in the right eye due to the presence of a corneal scar. The light reflex in the left eye was normal. Vision was impaired in the right eye only. The visual fields were grossly normal. The fundi appeared normal. The external ocular movements were normal in all fields of movement but there was a horizontal nystagmus of second degree on either lateral gaze. The corneal reflexes were normal and there did not appear to be any sensory abnormalities in any of the trigeminal fields. The facial expressional movements were equal. There was bilateral eighth nerve deafness, more pronounced on the right side. The gag reflex was present on both sides and the uvula and soft palate moved in the midline. The left shoulder was slightly lower than the right. The tongue protruded in the midline without tremor or atrophy. The speech, nevertheless, was quite thickened and almost indistinct. There was difficulty in swallowing fluids and, on occasion, the fluid would regurgitate through the nose.

The gait was markedly ataxic with falling to either side in the Romberg position. In attempting to walk, he would drag his right lower limb. The deep tendon reflexes were bilaterally exaggerated, but more so on the right side. There was a Hoffmann sign on the right side with bilateral Babinski responses, more easily elicited on the right side. There was marked weakness in motor power of the right upper and lower limbs. The motor weakness was mild on the left side. There was a bilateral dysmetria and dyskinesia of the upper limbs, more pronounced on the right side. Ataxia was pronounced in both lower limbs, but also was more exaggerated on the right side.

Sensory disturbances to pain and temperature were not distinct. However, he was able to appreciate an ice tube more acutely on the entire left side with a definite increase in sensa-

tion bilaterally at the level of the second cervical dermatomere. Vibration, position and stereognostic sense were unimpaired.

Laboratory Studies. The urinalysis and complete blood counts were normal. The spinal fluid and blood serology were normal. The blood calcium was 10.2 mgm. per 100 cc.; the blood phosphorus was 4.5 mgm. per 100 cc. while the alkaline phosphatase was elevated to 36 Bodansky units per 100 cc.

Roentgenograms. I am indebted to Dr. W. Edward Chamberlain for the following comments and descriptions of the roentgenologic findings in this case.

"Advanced Paget's disease of the skull and upper cervical spine is here visualized (Fig. 1). This is characterized by thickening of the bone with loss of demarcation of the outer table of the skull. Many small distinct and conglomerate areas of increased bone density are seen. These are characteristic of the disease.

FIG. 1. Right lateral projection of skull showing advanced Paget's disease with secondary platybasia (marked flattening of the "basal angle" between floor of anterior fossa and clivus) and basilar impression (invagination of occipital condyles, margins of foramen magnum and other basal structures into the brain space). In Paget's disease the bones become softened, even when their mineral content is high. The deformities here visualized are a result of that softening.

"Paget's disease produces marked softening of the bone, even in the presence of increased bone density (increased calcium content). As a result of this softening a marked degree of secondary basilar impression has developed. The cephalo-caudal dimension of the cranium is at least 2 cm. less than the normal. The angle between the floor of the anterior fossa and the clivus, normally of the order of 135 degrees, has flattened to approximately 160 degrees. The basilar invagination is most marked at the ventral margin of the foramen magnum, less marked at its dorsal margin. As a result of this, the plane of the foramen magnum is inclined dorsad and obviously there must be a kinking of the brain stem where it passes around the invaginated odontoid process and the ventral margin of the foramen magnum.

FIG. 2. Normally the plane of the foramen magnum is so disposed that this "high angle vertex projection" fails to visualize it. In basilar impression the invagination is more marked at the ventral margin of foramen than at the dorsal margin. Its plane thus becomes angulated so that it may be visualized by this angle of projection. When viewed in the stereoscope the outlines of the foramen can be readily distinguished. In this non-stereoscopic illustration its outlines may be confused with the more apparent somewhat concentric outlines of the upper vertebral canal.

"Normally the foramen magnum is best visualized roentgenographically in 'fronto-vertex projections' (central ray passing through head in midsagittal plane from nape of neck to a point approximately midway between the hairline and bregma) or in 'occipital projections' (central ray in midsagittal plane from hairline at top of forehead to region of foramen magnum). In the presence of this degree of basilar impression, due to the abnormal inclination of the foramen it is best visualized in 'vertex projections' (central ray in midsagittal plane from region of larynx and epipharynx to vertex of cranium), as shown in Fig. 2.

"Air introduced by lumbar puncture for encephalomyelography visualized an almost complete block, with the caudal limit of the cisterna magna and one of the cerebellar tonsils displaced down the vertebral canal as far as the upper borders of the laminae of C-3 (Fig. 3). Some air did enter the cranial cavity, indicating that the block was incomplete or inconstant, but even after prolonged maintenance of the sitting position, most of the air remained below the level of the foramen magnum."

Encephalomyelogram. Jan. 14, 1944. At the above-mentioned encephalomyelographic procedure the initial spinal fluid pressure was normal. The fluid was clear and all laboratory findings were nega-

FIG. 3. Left lateral projection of upper cervical canal after encephalomyelographic injection of air. As a result of the basilar impression, the subtentorial portion of the brain space has been encroached upon and a foraminal hernia has developed. The cisterna magna and right cerebellar tonsil have descended as far as the cephalic borders of the laminae of vertebra C-3.

tive. A partial block was indicated by manometric readings during jugular compression.

Operation. Jan. 18, 1944. Suboccipital craniectomy with high cervical laminectomy (Dr. H. Wycis). Under avertin-local anesthesia, the usual midline incision was made with reflection of the cervical and occipital muscles. The angle between the occiput and the upper cervical spine was so acute that it was very difficult to free the atlas and axis. The rim of the atlas on the right side was fused with the posterior rim of the foramen magnum. Of striking interest was the fact that the second cervical spinous process was extremely huge and porous. The bone had the consistency of cheese and was extremely vascular. It appeared so soft that the laminectomy could have been completed with a stout pair of scissors. The laminae of the first five cervical vertebrae were removed. The bone over the cerebellar hemispheres was then rongeured away. The dura was thickened and deeply indented over the cord in the region of the atlas. The dura was opened over the upper cervical segments and over both cerebellar hemispheres. It was noted that the tonsils of the cerebellum were herniated through the foramen magnum for a distance of approximately one inch with greater displacement on the right side than on the left. There was a suggestive Chiari deformity due to a kinking of the posterior part of the medulla against the upper cervical cord. It appeared as if the entire cervical cord and medulla were foreshortened because of the deformity. The second cervical roots were swung in a hammock fashion about the lower poles of the tonsils. The second cervical roots were crushed on both sides. The dura was allowed to remain open and the muscle layers were closed with interrupted steel wire. Skin was closed with silk.

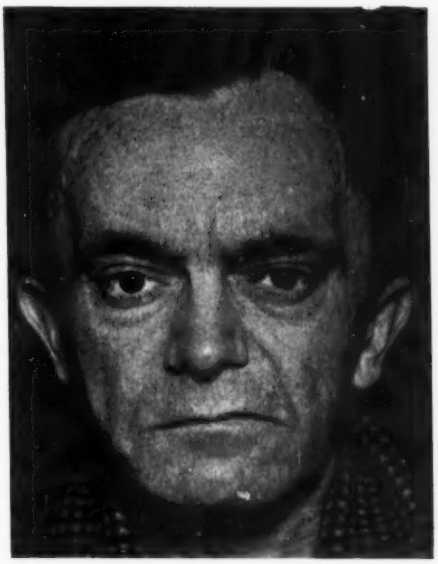


FIG. 4. Patient two weeks after operation. Note the prominent temporal vessels.

Postoperative Course. The postoperative course was little short of dramatic. Eight hours after operation he was alert and conscious. He stated that he had no occipital pain and that the numbness and tingling were absent from his hands and feet. Two weeks after operation he felt nearly normal. The pain had entirely subsided. He could walk without dragging the leg and the ataxia had almost completely abated. He stated that hearing had improved in the left ear. Speech was now distinct and there was a marked improvement in swallowing. Nystagmus was still present on either lateral gaze. The deep tendon reflexes were still more active on the right side with bilateral Babinski signs. Six weeks later, he presented few, if any, neurological abnormalities except for an equivocal Babinski on the right side. He was free of all pain, and had a substantial increase in appetite and gain in weight. There was an area of anesthesia over the distribution of the second cervical dermatomere due to the crushing of the second cervical posterior roots. Hearing, however, was apparently unchanged. The tortuosity of the temporal vessels had markedly decreased (Fig. 4).

Microscopic Examination. The bone removed shows the characteristic mosaic pattern of Paget's disease (Fig. 5).

COMMENT

A successful surgical result in a case of basilar impression secondary to Paget's disease is presented. The writer feels that wherever possible the

dura should be allowed to remain open so as to permit full decompression. List[9] likewise recommends opening the dura for adequate decompression. In the successfully operated case by Dr. Temple Fay (Chamberlain, Case I[2]) the dura was allowed to remain open.

The probability of other cases of basilar impression secondary to Paget's

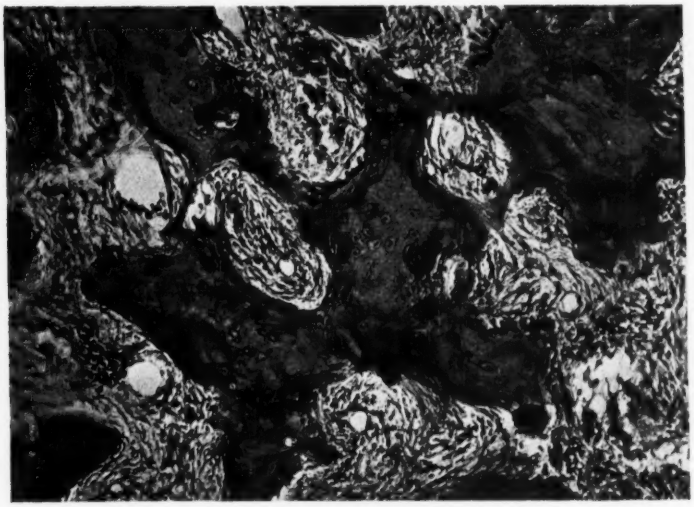


FIG. 5. Showing the characteristic mosaic pattern of Paget's disease.

disease certainly exists. Patients with Paget's disease should have thorough neurological examinations, as well as thorough X-ray studies of the upper cervical region and foramen magnum area. Since the writing of this report, the author has encountered two other cases of Paget's disease with neurological dysfunction due to compression by the diseased bone. In one case there was early bilateral loss of hearing, tingling in both hands and fingers, and unsteady gait. The X-rays of the skull show typical platybasia. The second patient presented himself with progressive loss of vision in the left eye due to compression of the optic nerve in the optic canal. Both patients refused operation.

REFERENCES

1. BOOGAARD, J. A. De indrukking der grondolakte van den schedel door de wervelkolom, hare oorzaken en gevolgen. *Ned. Tijdschr. Geneesk.*, 1865, *2:* 81–108.
2. CHAMBERLAIN, W. E. Basilar impression (platybasia). A bizarre developmental anomaly of the occipital bone and upper cervical spine with striking and misleading neurologic manifestations. *Yale J. Biol. Med.*, 1939, *11:* 487–496.
3. EBENIUS, B. The roentgen appearance in four cases of basilar impression. *Acta radiol.*, 1934, *15:* 652–656.
4. GRAWITZ, P. Beitrag zur Lehre von der basilaren Impression des Schädels. *Virchows Arch.*, 1880, *80:* 449–474.

5. Homén, E. A. Zur Kenntnis der rhachitischen (?) Deformationen der Schädelbasis und der basalen Schädelhyperostosen. *Dtsch. Z. Nervenheilk.*, 1901, *20:* 3–15.
6. Juhlin-Dannfelt, C. Platybasie. *Svenska Läkartidn.*, 1933, *30:* 470–473.
7. Kecht, B. Zur Kenntnis der Klinik eines Falles von basilarer Impression des Schädels. *Z. ges. Neurol. Psychiat.*, 1932, *141:* 132–140.
8. Krause, F. Chirurgie des Gehirns und Rückenmarks nach eigenen Ehrfahrungen. *Berlin: Urban & Schwarzenberg*, 1911, *2:* 556–558.
9. List, C. F. Neurologic syndromes accompanying developmental anomalies of occipital bone, atlas and axis. *Arch. Neurol. Psychiat., Chicago*, 1941, *45:* 577–616.
10. Merio, P., and Risak, E. Klippel-Feilsches Syndrom, basilare Impression und endokrine Erkrankungen. *Z. klin. Med.*, 1934, *126:* 455–468.
11. Rokitansky, C. Cited by Ebenius.
12. Schüller, A. Zur Röntgen-Diagnose der basalen Impression des Schädels. *Wien. med. Wschr.*, 1911, *61:* 2594–2599.
13. Sinz, P. Unterentwicklung des Hinterhaupt- und Keilbeinkörpers mit gleichzeitiger knöcherner Verbindung zwischen Atlas und Schädel als Todesursache. *Virchows Arch.*, 1933, *287:* 641–650.
14. Virchow, R. Beiträge zur physischen Anthropologie der Deutschen, mit besonderer Berücksichtigung der Friesen. Reprinted from: *Abh. Akad. Wiss., Berlin, 1876.* Berlin: F. Dümmler, 1877, 390 pp.
15. Walsh, M. N., Camp, J. D., and Craig, W. McK. Basilar invagination of the skull (so-called platybasia): report of a case with operation. *Proc. Staff Mayo Clin.*, 1941, *16:* 449–452.

HISTOLOGIC STUDIES OF THE BRAIN FOLLOWING HEAD TRAUMA

IV. LATE CHANGES: ATROPHIC SCLEROSIS OF THE WHITE MATTER

JOSEPH P. EVANS, M.D., AND I. MARK SCHEINKER, M.D.

The Laboratory of Neuropathology, Cincinnati General Hospital, and the Department of Surgery, University of Cincinnati College of Medicine, Cincinnati, Ohio

(Received for publication May 18, 1944)

IN THREE PREVIOUS communications[4,5,6] we have described our interpretation of the mechanism by which certain early traumatic lesions of the central nervous system are produced: cerebral edema, petechial and massive hemorrhages in the central areas of the brain, and infarction of several of the major cerebral arteries.

It is the purpose of the present paper to report our findings in a series of cases displaying late histologic changes in which were found smaller and larger areas of atrophic sclerosis of the white matter, and to discuss the pathogenesis of these lesions.

PRESENTATION OF CASES

Case 1. *Short period of unconsciousness following a head injury. Development of sulfathiazole nephrosis with death at the end of 12 days. Autopsy showed the presence of nephrosis and, in the brain, multiple areas of softening.*

History and Course. H. W., a 56-year-old colored male, was admitted to the hospital unconscious shortly after having been struck by a bus. The significant findings were a laceration over the left eye, a fractured mandible, and fracture of the sixth and seventh ribs. Save for loss of consciousness, which was regained shortly after admission, neurologic examination was negative. He was placed under observation and, because of the scalp wound and jaw fracture, sulfathiazole therapy was instituted. For nine days he improved, then there occurred elevation of temperature and an increase in the pulse and respiratory rates. It was thought possible that a subdural clot had developed but exploratory burr holes revealed none.

The next day red blood cells were found in the urine and sulfathiazole therapy was stopped. However, it soon became apparent that uremia was developing. The blood urea nitrogen concentration rose to 136 mg., and then to 200 mg. per 100 cc. of blood. Cystoscopic examination and ureteral drainage showed no sulfathiazole crystals, so that it was concluded that he was suffering from sulfathiazole nephrosis. He died 12 days after admission.

Necropsy Findings. These, exclusive of those in the nervous system, were sulfathiazole nephrosis, acute cystitis, urethral strictures, and fracture of the left temporal bone, the left mandible, and the third and fourth ribs on the right.

Gross Anatomic Observations. The dorsal surface of the brain was flattened, and the leptomeninges were slightly thickened. The undersurface of the brain appeared normal. The blood vessels at the base were soft save for scattered areas of mild sclerosis. On coronal section there were found multiple scattered areas of petechial hemorrhage, chiefly in the white substance. No areas of massive hemorrhage or grossly visible softening were present.

Microscopic Observations. Blocks were taken from various areas of the cerebral cortex, from the basal ganglia, and the hypothalamus. There were found diffusely scattered small areas of softening and vascular alterations.

The areas of softening varied greatly in size and shape, and consisted of accumulations of compound granular cells. Some scavenger cells contained blood pigment. Occasionally larger

areas of softening were seen in which gitter cells and newly formed blood capillaries replaced the destroyed brain tissue. Some of the foci of softening were in the vicinity of blood vessels which disclosed definite signs of stasis and congestion (Fig. 1). The smaller veins and capillaries appeared distended and engorged with blood, and in some of the congested veins the walls were undergoing disorganization and necrosis. Some of them were surrounded by distended perivascular spaces filled out with large accumulations of red blood cells. Occasionally they contained small numbers of gitter cells. Congested veins were present throughout the entire hemisphere, especially in the white matter. Some were surrounded by perivascular hemorrhages, or by circumscribed areas of edema and rarefaction of the adjacent tissue.

Case 2. *Head injury from blunt object. Previous injury 17 years earlier. Recent blow was at*

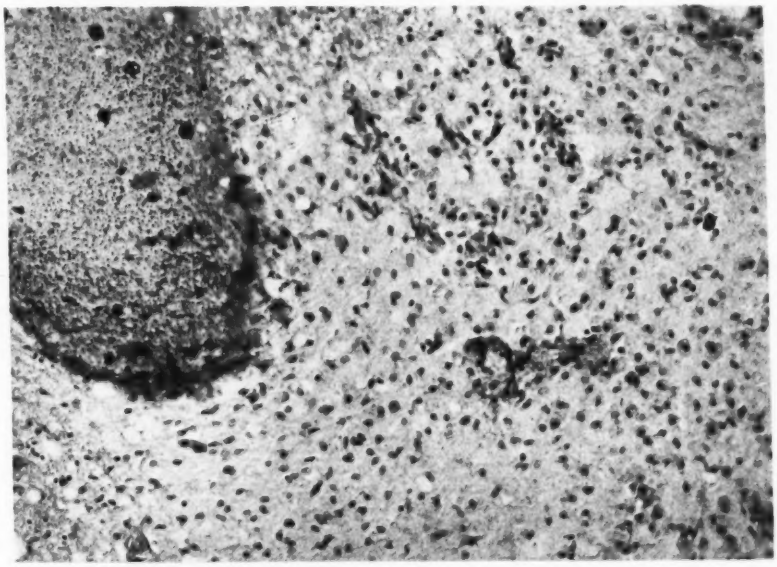


FIG. 1. *Case 1.* Small area of softening in which gitter cells and newly formed capillaries replaced the destroyed brain tissue. Note the tremendous distention and stasis of the smaller veins. Hematoxylin and eosin (×165).

site of old decompression. Flaccid hemiplegia led to exploration for subdural clot; none found. Intracerebral clot later evacuated. Staphylococcus septicemia secondary to carbuncle. Death in 50 days. Extensive changes in the vicinity of the intracerebral clot.

History and Course. R. H., a 36-year-old colored male, was admitted to the hospital about two hours after being struck in the left parietal region with a blunt object. Seventeen years earlier he had sustained a head injury in the treatment of which a large parietal decompression was made.

On admission he was unconscious. In the old decompression area were found two superficial abrasions and a large subgaleal hematoma. There was a right-sided flaccid hemiplegia. Because of the hemiplegia, exploratory burr holes were made on the first hospital day in search of a possible subdural hematoma. None was found. On the third day ventriculograms gave evidence of a left frontal lobe hemorrhage. A small bone flap was reflected, and 35 cc. of blood were evacuated from the left frontal lobe. He improved gradually following this procedure,

but remained severely dysphasic. A carbuncle developed in the right shoulder and septicemia followed, from which he died on the 50th hospital day.

Gross Anatomic Changes. Figure 2 shows the general nature and extent of the destructive lesion in the left fronto-parietal region. There were large areas of tissue softening, surrounded

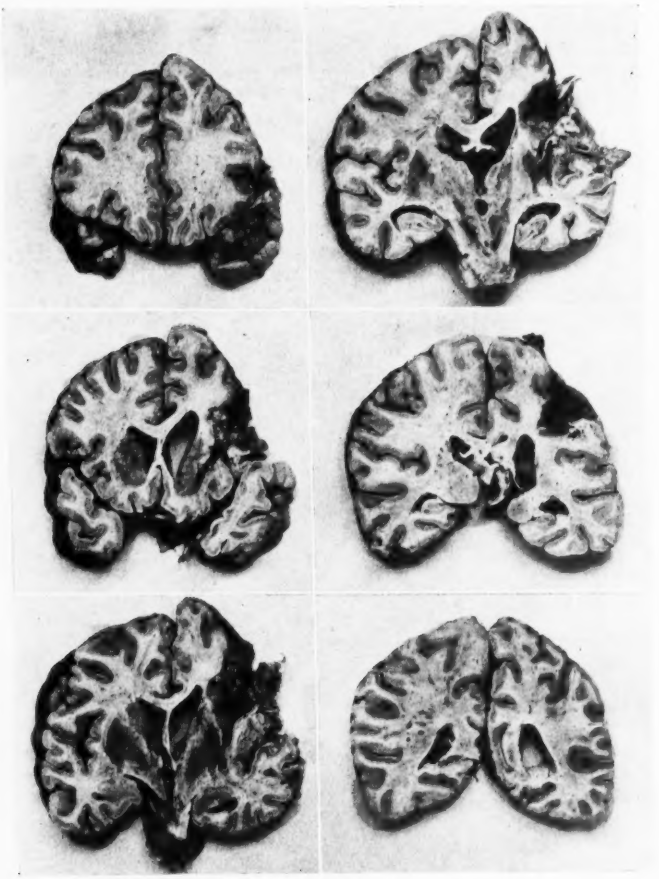


FIG. 2. *Case 2.* Large areas of tissue destruction in the left fronto-parietal region, associated with intracerebral clot.

by a thin margin of golden-brown discoloration. The area involved extended deep into the white matter and measured in its greatest diameter 5 × 2 cm. The leptomeninges over the area of destruction were thickened and stained yellowish-brown.

Transverse sections through the pons and cerebellum showed discrete areas of diffusely scattered diapedetic hemorrhages.

Microscopic Observations. Blocks were taken from the left fronto-parieto-temporal region and were stained with hematoxylin and eosin, and phosphotungstic acid. Frozen sections from

the same region were impregnated by the Hortega silver carbonate and the Cajal gold chloride methods.

Examination showed slight fibrous thickening of the parietal leptomeninges which contained numerous macrophages filled with blood pigment. The pial vessels were congested and surrounded by large masses of extravasated red blood cells. The principal alteration within the brain itself consisted in numerous areas of tissue destruction typical of far advanced softening. The greater part of the cortex appeared completely destroyed and replaced by large masses of gitter cells in a dense network of newly formed capillaries. It was of interest that in areas distant from the softening the vessels appeared congested and disclosed signs of stasis

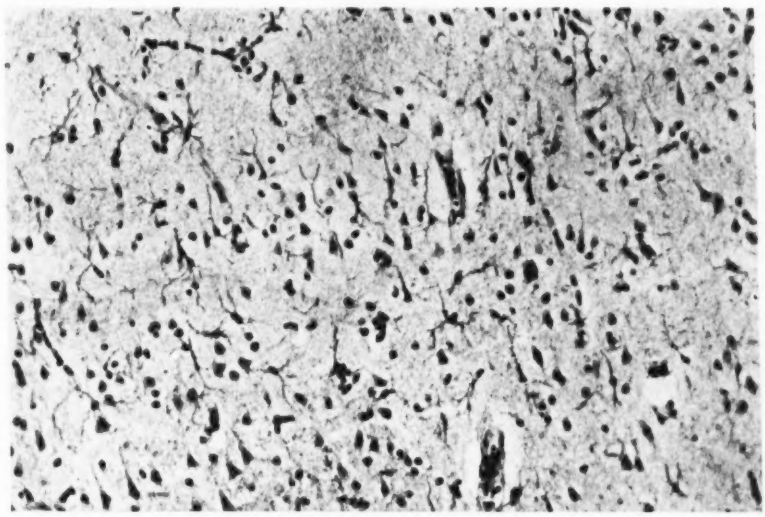


FIG. 3. *Case 2.* Increased amount of microglial elements throughout the areas adjacent to the softening. Hortega's silver carbonate impregnation (×165).

and prestasis. The perivascular spaces were distended and the adjacent tissue appeared rarefied and edematous. Many of the nerve cells were lost while others showed severe cell changes and ischemic degeneration.

Sections stained with phosphotungstic acid disclosed an increase in fibrous tissue outlining the greater portion of the area of softening. In addition there was a slight increase in glial fibers, more particularly toward the surface of the destroyed area. There was some increase in the subpial glial tissue. The blood vessels in the region adjacent to the area of softening showed an increase in adventitia. No definite sclerosis or thrombus formation was seen in any of the vessels. There was a striking increase in microglia throughout the areas adjacent to the softening (Fig. 3).

In sections prepared by Cajal's gold sublimate method, many hypertrophied astrocytes were seen in the outer border of tissue around the area of softening (Fig. 4). Here, in the area of tissue destruction, many of the astrocytes displayed clasmatodendrosis. Obviously the bulk of these changes was the result of the 50-day-old injury, rather than that sustained 17 years earlier, though some of the glial hypertrophy may have been longstanding.

Case 3. *Severe head injury in 1935. Readmission in 1937 with focal seizures. Further admissions, and finally death in 1941 in status epilepticus. Extensive cerebral atrophy and gliosis.*

History and Course. J. B. was first admitted to the hospital in 1935 at the age of 49, an

indefinite period of time following an injury to his head. He was restless and somewhat stuporous. There was found an old non-infected healed scalp laceration. Neurological examination showed no localizing signs. The cerebrospinal fluid was grossly bloody and the pressure was reported as "increased." The blood and cerebrospinal fluid Wassermann reactions were negative, and the gold curve was reported as 0^{10}. On bed rest he improved rapidly and was discharged on the 13th day.

In 1937 he was readmitted because of left-sided convulsive seizures associated with transient post-convulsive left hemiparesis. The diagnosis of arteriosclerotic heart disease was made at this time. There followed a series of admissions because of recurrent seizures. Pneumoencephalograms in 1939 showed evidence of diffuse cerebral atrophy, far advanced in the

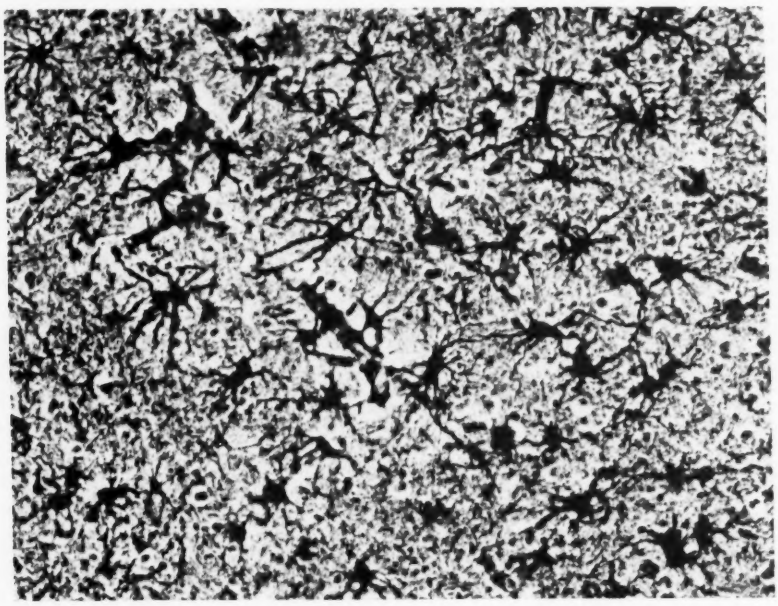


FIG. 4. *Case 2.* Proliferation and hypertrophy of astroglia especially marked in the white matter of the left centrum semi-ovale. Cajal's gold sublimate method (×235).

right hemisphere. There was displacement of the third ventricle to the right, but a focal contracting lesion was not demonstrable. When placed on dilantin he showed temporary improvement, but on October 8, 1941, he was brought to the hospital because of rapidly repeated left-sided Jacksonian seizures. Death followed four days later.

Postmortem examination showed bronchitis, lobular pneumonia affecting both lower lobes, and arteriosclerosis of the aorta.

Gross Anatomic Observations. The right hemisphere was smaller throughout than the left. The undersurface of the right frontal lobe showed loss of substance and brownish discoloration.

The coronal sections are shown in Fig. 5. The loss of bulk in the right hemisphere and the compensatory dilatation of the right ventricle are evident.

Microscopic Observations. Blocks were taken from the right frontal region (upper, lower, mesial, and lateral surfaces), right centrum semi-ovale, right ventricular wall, and hypothala-

mus. They were stained with hematoxylin and eosin, and phosphotungstic acid, and by the Loyez and Bodian methods. Frozen sections were taken from the right frontal region and prepared by the Cajal gold sublimate and the Hortega silver carbonate methods.

In the dorso-lateral portion of the right frontal lobe were several abnormalities. The subarachnoid spaces were distended and showed moderate connective-tissue proliferation. The cortical ribbon was relatively well preserved, though small areas of glial scarring were evident.

The most striking changes were in the white matter, which disclosed throughout the sections an increase in astrocytic nuclei. In some regions the glia appeared as an extensive scar. These changes were especially prominent in the regions in which the parenchymatous cortical

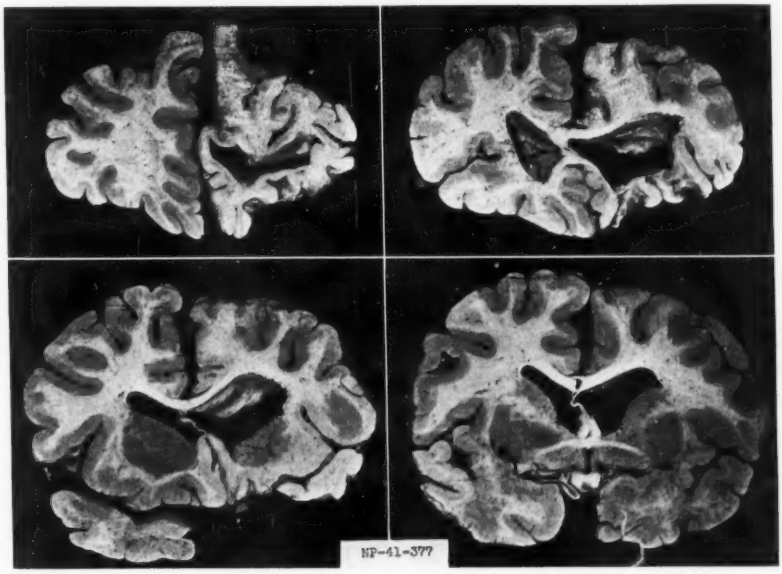


FIG. 5. *Case 3.* Diffuse loss of bulk in the right hemisphere with dilatation of the right ventricle.

changes were slight or absent. It is of interest to note that the nervous tissue adjacent to some of the blood vessels disclosed a high degree of rarefaction amounting to perivascular cystic formation (Fig. 6). These zones often contained pigment-bearing macrophages.

Sections stained with phosphotungstic acid showed diffuse proliferation of glial fibrils throughout the white matter. The fibrils in the gray matter appeared fairly well preserved except in the molecular zone, where they were increased and some appeared thicker than normal.

In sections stained by the Loyez method, there was found diffuse loss of myelin in the white matter with sparing of the cortical ribbon. In some areas the "u" fibers as well as the fibers adjacent to the ventricular wall appeared relatively well preserved. Under higher magnification the myelin sheaths displayed various types of destruction: swelling, beading, and fragmentation.

Sections impregnated by the Bodian method disclosed a moderate degree of axis-cylinder

damage in the form of bead-like swelling, slight tortuosity, and occasional fragmentation of the affected axones.

The dorso-mesial portion of the right frontal lobe disclosed findings in the gyrus cinguli similar to those described above. It is of interest to note that the adjacent areas in the corpus callosum and mesial portions of the frontal cortex were fairly well preserved, suggesting that any changes due to circulatory disturbance were not the result of disturbance in the supply of the anterior cerebral artery, but rather were of local character.

In summary the changes consisted of sclerotic atrophy of the entire right frontal lobe with compensatory dilatation of the right lateral ventricle. There was proliferation of fibril-

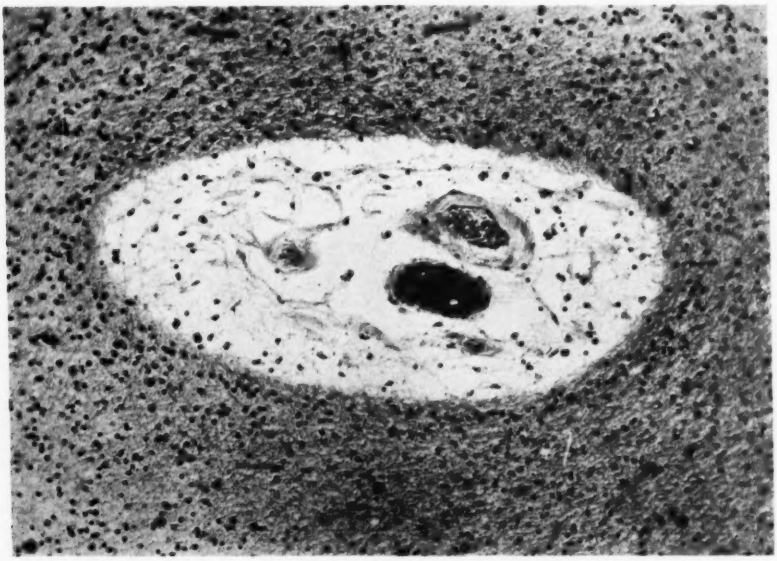


FIG. 6. *Case 3.* Perivascular tissue rarefaction amounting to small cyst formation. Note the increased amount of glial nuclei throughout the white matter. Hematoxylin and eosin (×135).

lary astrocytes throughout the centrum semi-ovale of the right frontal lobe, associated with a diffuse demyelination and mild degenerative changes of the axis cylinders. The cortical ribbon escaped significant change except in the basilar gyri where presumably it was subjected to direct contusion and laceration.

Case 4. *Severe head injury followed by a three weeks' period of unconsciousness. Development of signs of dysphasia led to evacuation of a subdural hematoma. Lung abscess developed. Death occurred three years later. Brain showed extensive old damage of the left hemisphere.*

History and Course. P. L., a 54-year-old colored male, had enjoyed apparently excellent health until about September 1, 1939, when he was struck by a bus, rendered unconscious, and taken to another hospital. There he lay unconscious for three weeks. Roentgenograms showed an occipito-temporal fracture on the right, running into the basilar region. At the end of the second week, lumbar puncture was done. It was reported that there was no blood in the cerebrospinal fluid. The cerebrospinal fluid Wassermann was positive, and a paretic gold curve was found. Further data were not obtained. By the end of the fifth week he had improved somewhat, but was thought to be psychotic. Therefore he was transferred to the

Psychiatric Service of the Cincinnati General Hospital, where he was admitted on October 5, 1939 with the diagnosis of general paresis.

It was soon appreciated that he was not demented but dysphasic; and a lung abscess was found.

It was thought that post-traumatic cerebral atrophy was a more likely diagnosis than subdural hematoma, but in view of the localizing sign of dysphasia, a left-sided burr opening was made and "a moderate amount of thin, slightly yellowish, discolored fluid under moderate pressure" was evacuated. The brain was depressed about one-quarter of an inch from the calvarium. Similar findings were made on the right side. He improved very little following the evacuation of the hematomata; his pulmonary condition became more severe and he was bronchoscoped without benefit. Because of his mental status (due in large part, no doubt, to his dysphasia), arrangements were made for his commitment to the State Psychiatric Hospital. At this time lumbar puncture revealed an initial pressure of 0 (*sic*), the total protein was 22 mg. per cent, the cerebrospinal fluid Wassermann and gold curve reactions were negative. Shortly before his discharge, he had a number of ill-defined convulsive seizures, and was placed on dilantin.

Death occurred about three years following his discharge from the General Hospital and about three years and four months following his injury. An interim history is not available, nor have we information concerning the general findings at autopsy.

Gross Anatomic Changes. The undersurfaces of both leaves of the dural cap showed traces of the old hematoma membrane. There was extensive atrophy of the left hemisphere, particularly in the peri-Sylvian region where a strip of destruction, 3 cm. wide and 5.5 cm. in length, extended along the course of the Sylvian vessels. The vessels at the base of the brain were thin-walled and the configuration of the circle of Willis was normal.

The brain stem and cerebellum revealed no gross abnormalities.

Microscopic Observations. Blocks were taken from various areas of the left hemisphere. There were large areas of old cystic softening involving chiefly the gray matter. These probably were the result of local damage, though since knowledge of the mechanism of the injury and early clinical data are lacking, this cannot be maintained with complete assurance.

The change of particular interest, however, was the diffuse sclerosis of white matter similar to that described in Case 3. The entire centrum semi-ovale showed a diffuse increase in astrocytic nuclei. In some areas, well beyond the obvious gross changes, the glia appeared as an extensive scar. Dense fibrillary glia was present throughout the white matter adjacent to the lateral ventricle. It should be emphasized that these glial changes were seen in regions where the cortical ribbon did not appear severely damaged.

Case 5. *No history. Death twelve days after admission to hospital. Autopsy showed signs of old post-traumatic cerebral damage.*

History and Course. T. B., a 63-year-old white man, was picked up intoxicated and unconscious by the police. No history could be obtained. The positive physical findings were: blood pressure 180/110, flaccidity of the left side including the face, hyperactive tendon reflexes on the left, positive Hoffmann and Babinski responses bilaterally, and evidence of early cardiac failure.

He was digitalized and given general supportive treatment and sulfathiazole. He gradually regained consciousness, but remained aphasic. During the twelve days of his hospital stay, his blood urea nitrogen level rose from 19 to 242 mg. per 100 cc., and his clinical course paralleled the rise in the blood urea nitrogen. The sulfathiazole level was 15.9 mg. per 100 cc. for four days before his death. The urine on one occasion showed a few sulfathiazole crystals, but never any red blood cells. He expired on the twelfth hospital day.

It was thought at the time of his death that he had suffered massive cerebral hemorrhage on the right (having had a probable old hemorrhage on the left), and that he had hypertensive cardiovascular disease. The question of kidney damage from sulfathiazole was raised.

The present interest centers chiefly about the fact that the autopsy findings indicated an old head injury, a history of which was not elicited.

Gross Anatomic Changes. The ventral surface of the brain showed several changes of

interest. In the region of the left Sylvian fissure there was extensive superficial loss of tissue with thickening of the leptomeninges and a golden-brownish discoloration. This discoloration extended across the Sylvian fissure and involved the anterior portion of the second temporal

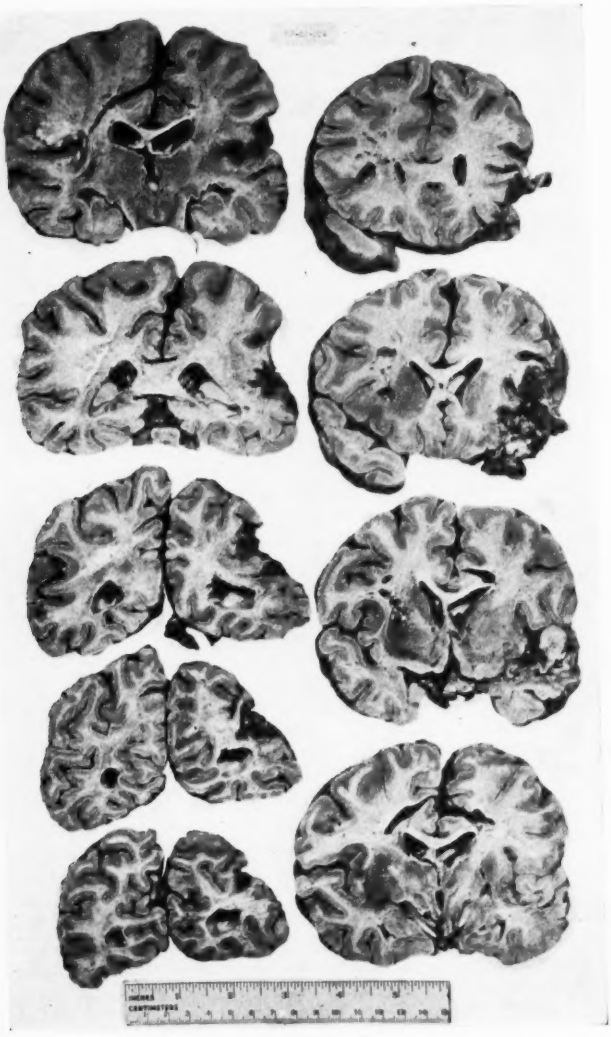


FIG. 7. *Case 5* Diffuse loss of substance in the left frontal and parietal lobes. Recent softening in the distribution of the right middle cerebral artery (island of Reil).

gyrus. The undersurface of the frontal lobe near the midline also showed a golden-brown discoloration and there was a small area of destruction in the right frontal lobe just beneath the olfactory bulb.

Horizontal sections through the hemispheres demonstrated diffuse loss of substance in the left frontal and parietal lobes (Fig. 7). In addition there was a recent softening in the distribution of the right middle cerebral artery extending downward throughout the island of Reil and across the external capsule to involve a small portion of the lateral extent of the putamen.

Microscopic Observations. Blocks taken from the left frontal lobe revealed the leptomeninges to be slightly thickened, but otherwise not remarkable. The cortical ribbon was generally well preserved, except for small circumscribed areas of old destruction. The striking findings were to be seen in the white matter, and consisted of a diffuse proliferation of glial nuclei and fibrils producing a widespread gliosis. In some areas both progressive and regressive glial changes were present, though the former usually predominated. There were dense bands of glial tissue in areas subjacent to the superficial tissue destruction. Regressive glial changes were limited to relatively small areas of the white matter. Oligodendroglial cells occasionally showed acute swelling. The microglia did not appear altered.

Case 6. *Subdural hematoma. Evacuated three days after injury. Three years later readmission because of convulsions. Death. Brain showed extensive localized gliosis.*

Course and History. O. H., a 60-year-old colored male, was readmitted to the hospital because of convulsions. Three years previously he had fallen and struck his head on a sidewalk. Three days following the accident, because of the presence of dysphasia, exploratory trepanation was performed and a left-sided subdural hematoma was evacuated through a subtemporal opening. The cavity left was of about 30 cc. capacity. The underlying brain was "somewhat reddish in color." Following his discharge a month later he was not seen again until the second admission.

Four days prior to readmission he had had a generalized convulsive seizure without apparent precipitating cause. The attacks recurred frequently, several times an hour on one day. Nevertheless, the day before readmission he was up and about, talking rationally and displaying no weakness. That night he had some thirty seizures, remaining unconscious between them. The attacks were said to be generalized, but there was more movement on the right.

He gradually improved and regained consciousness, though he remained mildly disoriented. An occasional convulsive movement was noted in the right hand. Then rather suddenly he developed signs of pulmonary edema, became comatose, and had several convulsive seizures. On the third hospital day sulfathiazole therapy was instituted, and by the seventh day the level had risen to 17 mg. per 100 cc. of blood despite attention to fluid. The blood urea nitrogen rose to 77 mg. per 100 cc. of blood. The urine remained clear save for the appearance of albumin. On the 10th hospital day he died.

Gross Anatomic Changes. The superior surface of the left frontal pole showed massive discoloration and disorganization extending back practically to the Rolandic fissure. The leptomeninges and underlying brain were stained a deep orange-brown, and the meninges were thickened, tough, and firmly attached to the brain. The undersurface of the left frontal and temporal lobes showed similar changes.

The brain was sectioned horizontally. The white matter of the left frontal lobe was shrunken and destroyed, and the overlying cortex was much depleted (Fig. 8). The anterior horn of the left lateral ventricle was correspondingly enlarged. There was diffuse gliosis at the junction of the gray and white matter. The right frontal lobe showed similar changes. The rest of the hemispheres appeared normal. The vessels making up the circle of Willis appeared normal in structure and distribution.

Microscopic Findings. Blocks were taken from various areas of the left frontal lobes. They revealed cystic softening of the cortical ribbon, seemingly the result of direct contusion and laceration. There were diffuse changes in the white matter, evidenced by proliferation and hypertrophy of the glial elements, particularly the fibrillary and protoplasmic astrocytes. The latter showed definite hypertrophy. The tissue generally appeared somewhat rarefied. No vascular or inflammatory lesions were found.

Case 7. *Admission in semi-coma in 1940 as the result of skull fracture. Subsequent convulsions. Readmission four months later in shock. Death from ruptured peptic ulcer. Autopsy revealed evidence of old brain trauma.*

History and Course. J. H., a 62-year-old white male, was admitted to the hospital on November 22, 1940 in coma. A later history revealed that his past health had been excellent. He had been a heavy drinker for 25 to 30 years and had been on a spree shortly before admission. He was not able to account for the hours immediately antecedent to his arrival in the hospital

Examination on admission showed a semi-comatose individual with a slightly dilated left pupil, bilateral optic atrophy, left facial paresis, and a left Hoffmann sign. Shortly thereafter a number of convulsive seizures were witnessed. These seemed to be generalized. Lumbar puncture revealed an initial pressure of 130 mm. of water. There were two white blood cells

FIG. 8. *Case 6.* Diffuse changes of the subcortical white matter of the left frontal lobe.

and eleven red blood cells per c.mm. Total protein content was 70 mg. per 100 cc. The Wassermann reaction of the blood was negative, as were also the cerebrospinal fluid Wassermann and gold curve reactions. Blood urea nitrogen was 18 mg. per 100 cc. Roentgenograms of the skull showed a large linear skull fracture in the right parietal region. This was the only frank sign of trauma obtained.

The convulsions ceased shortly after admission. His level of consciousness improved and after two weeks' hospital stay he was discharged with the diagnosis of chronic alcoholism associated with mental deterioration and convulsive seizures.

On March 14, 1941 he was readmitted in shock and died two hours thereafter. The diagnosis made at the autopsy table included duodenal ulcer with massive hemorrhage, generalized vascular sclerosis, and recent skull fracture of the right temporo-parietal region with focal extradural hemorrhage and evidence of old extensive brain injury.

Gross Anatomic Changes. In the right posterior parietal region there was a thin intradural clot, 3 cm. in width and 8 cm. in length.

The brain itself showed old brown staining over the dorsal surfaces of the frontal poles, and at the tip of the left frontal pole an old area of contusion, measuring 1.5 cm. in diameter. In the very tip of the right frontal pole was a similar change. The lateral surface of the temporal lobes likewise showed old brownish staining and some destruction of the underlying gyri. Similar brownish discoloration was found on the undersurface of the frontal and cerebellar lobes.

Microscopic Findings. Blocks from the right temporal lobe were studied. The leptomeninges showed patchy areas of fibrosis, containing fibroblasts, endothelial cells, and pigment containing macrophages. The cortex presented a few small areas of circumscribed tissue destruction. In addition there was found a more general patchy loss of nerve cells, particularly in layers 3 and 5, and here there were evident satellitosis and neuronophagia. Many shrunken and faded cells were seen in these areas.

The most striking changes, however, were found in the subcortical white matter. These consisted of a diffuse increase in glial cells and fibrils, similar to that described in the foregoing cases, resulting in extensive areas of fibrous gliosis.

COMMENT

We have been concerned in the present paper with the late atrophic changes that follow brain injuries. The case reports presented have been included chiefly to attest to the validity of the trauma. A number of authors have described the focal changes associated with cerebral cicatrix, notably Foerster and Penfield,[9] and Penfield.[10,11] Their concern has been with local changes, ours has been with the explanation of the diffuse cerebral atrophy evidenced, for example, by pneumoencephalograms made at various stages following the receipt of trauma.

In earlier papers we have discussed the acute changes following brain injury, emphasizing particularly the vascular alterations which we believe to be so largely responsible for both acute and chronic alterations in structure. Thus we have postulated and brought evidence to support the thesis that the earliest changes following injury consist in the escape of intravascular fluid through the paretic vessel walls with the production of edema. When the vasoparesis is of a severer grade there may occur escape of erythrocytes (and leukocytes) giving rise to perivascular hemorrhages. Both of these conditions cause an increase in fluid content of the affected cerebral tissue and if the process be limited chiefly to one hemisphere, shift of the ventricular system toward the opposite side will result during the acute stage.

Particular emphasis should be laid upon the fact that it is within the deeper structures of the cerebral white matter that these vasoparetic phenomena are believed to take place. And a sharp distinction must be made between the vascular alterations occurring in the deeper portions of the brain and those that are obviously the result of direct contusion and laceration of cerebral tissue at the surface.

It is evident that in instances of acute change, there must occur varying degrees of interference with transfer over the blood brain barrier. We have for facility of reasoning argued in terms of oxygen and carbon-dioxide trans-

port. Actually the problem is no doubt more complex and is related to fundamental cellular metabolism.

The late changes of such disturbed metabolism result, we believe, in the loss of neuronal elements, the severity of which is directly related to the degree of hypoxia (or a more profound metabolic alteration) resulting from the injury. On the other hand, astrocytes, unlike the nerve cells, hypertrophy in response to lesser degrees of oxygen want and disappear only as the oxygen want becomes severe.[3] Hence, in the later stages, as exemplified in the cases here presented, there is extensive neuronal loss, but as an index of the diffuse vascular alteration there occurs a diffuse gliosis which appears to be most severe in that area least well fortified to withstand vascular insults, the white matter. This portion of the brain has numerically fewer vessels and physiologically lesser capacity for the establishment of collateral channels.*

As demonstrated in these cases, direct contusion and laceration of the gray matter may be associated with profound changes in the cortical ribbon. Presumably in these instances the cortical circulation has been grossly and extensively disorganized, but in these same instances there are to be found diffuse glial changes throughout much of the adjacent white matter.

We have discussed in detail in earlier papers the nature and pathogenesis of these diffuse alterations in the white matter. By way of recapitulation their hypothetic basis may be described as follows. As the result of injury to the brain, noxious stimuli are transmitted to the vessels of the white matter. These stimuli appear to cause either direct relaxation of the muscular coat of the smaller vessels, or to result in the propagation of vasoparetic stimuli over the neurovascular network to the deeper vessels. It may be, as suggested by Ferris,[8] that the difference between the viscosity of the fluid blood and the fluid matrix of the nervous parenchyma facilitates the production of vasoparesis.

We postulated that the stasis so regularly seen in our cases in the smaller peripheral subdivisions of the vascular tree was the result of vasoparesis, and that the stasis with its associated accumulation of carbon dioxide led to further dilatation, to greater stasis, and eventually to the development of edema. Should the stasis become more severe, actual necrosis and softening of the parenchyma might occur. Should, on the other hand, the inadequacy of blood supply be less severe, and should it be present for a relatively long period of time, the development of atrophic sclerosis of the white matter, as

---

* The relatively greater susceptibility of the white matter to lesions caused by circulatory disturbances is a point worthy of additional comment. It has been noted by Bodechtel[1] in two cases of chronic cardiac decompensation, and by Ferraro[7] using as an experimental asphyxial poison sub-lethal doses of cyanide. Both observers found the gray matter essentially normal. Similar findings were observed by one of us (I.M.S.) in the brain of a patient who died of carbon monoxide poisoning, and also in the brain of a child, which showed diffuse sclerosis of the white matter, apparently due to vascular disturbances. A more detailed description of this interesting discrepancy between the reaction of gray and of white matter to circulatory disturbance will be described in detail elsewhere.

described in the cases embodied in this report, might reasonably be expected to occur.

That alterations occur in the gray matter is not to be denied. We believe, however, that the more severe forms of gray-matter disturbance occur as the result of direct contusion, or as the result of grave disturbance in the circulation of major arterial trunks.[6]

We have attempted to correlate our observations with the pneumoencephalograms of patients who have suffered head injury. In our experience in civilian practice diffuse enlargement of the ventricles is a more common finding than focal dilatation of a part of the ventricular system, which we believe correlates well with the more usual gross and histologic changes. In military practice, however, the occurrence of focal lesions is much more frequent, and it was chiefly upon a study of such material that Foerster and Penfield drew their conclusions concerning the wandering of the ventricles toward the site of local injury. They postulated that the shift occurred as the result of contraction of the local cicatrix. That this need not always be the explanation is indicated by the fact that one of us (JPE) has seen appreciable ventricular shift in an experimental animal as early as three weeks following the production of an extensive cerebral wound, before there was time for the development of cicatrization. It would seem that as atrophy of one hemisphere occurs in asymmetrical lesions, there is a tendency for the normal ventricle to shift toward the affected side, helping to fill the vacated space, and resulting in a less great compensatory dilatation of the ipsilateral ventricle than would otherwise occur. Because of the rigid falx of the adult the shifting of the more normal hemisphere is never so great as in the case of an infant, whose falx is relatively mobile up to the age of about one year.

Dyke[2] likewise believed that local dilatation of a ventricle and shift of the intracranial contents occur in an effort to compensate for loss of brain bulk.

SUMMARY

The pathologic alterations in the brains of seven patients surviving head injuries for variable periods of time up to seventeen years have been analyzed.

We have been concerned not with the focal changes associated with cerebral cicatrix but rather with seeking an explanation of diffuse cerebral atrophy noted following many forms of head injury.

Attention is called to the evidence of stasis in the smaller blood vessels, and the associated edema and perivascular hemorrhages, notably in the white matter. We believe that as a result of these circulatory alterations hypoxia develops. In the cases described the circulatory disturbances have been relatively longer lived and as a result diffuse gliosis of the white matter has developed, since the characteristic reaction of glia to sustained oxygen want of moderate degree is gliosis. That some loss of neuronal elements occurs is true, but the changes are relatively greater in the white matter which is less well equipped to withstand vascular insults.

The resultant pneumoencephalographic changes are discussed and an explanation sought for them. Diffuse atrophy is thought to be a more significant factor than focal cicatrix in the production of ventricular wandering.

REFERENCES

1. Bodechtel, G. Gehirnveränderungen bei Herzkrankheiten. *Z. ges. Neurol. Psychiat.*, 1932, *140:* 657–709.
2. Dyke, C. G. The roentgenological aspects of fractures of the skull and injuries of the brain. In: *Injuries of the skull, brain and spinal cord. Neuro-psychiatric, surgical, and medico-legal aspects.* S. Brock, Ed. Baltimore: Williams and Wilkins Co., 1943, 2nd ed., 383–419.
3. Evans, J. P., and McEachern, D. The circulatory changes in cerebral vascular occlusion and in cerebral cicatrization. *Res. Publ. Ass. nerv. ment. Dis.*, 1937, *18:* 379–391.
4. Evans, J. P., and Scheinker, I. M. Histologic studies of the brain following head trauma. I. Post-traumatic cerebral edema. (To be published).
5. Evans, J. P., and Scheinker, I. M. Histologic studies of the brain following head trauma. II. Post-traumatic petechial and massive intracerebral hemorrhages. (To be published)
6. Evans, J. P., and Scheinker, I. M. Histologic studies of the brain following head trauma. III. Post-traumatic infarction of cerebral arteries, with consideration of the associated clinical picture. *Arch. Neurol. Psychiat., Chicago*, 1943, *50:* 258–278.
7. Ferraro, A. Experimental toxic encephalomyelopathy (diffuse sclerosis following subcutaneous injections of potassium cyanide). *Psychiat. Quart.*, 1933, *7:* 267–283.
8. Ferris, E. B. Personal communication to the authors.
9. Foerster, O., and Penfield, W. Der Narbenzug am und im Gehirn bei traumatischer Epilepsie in seiner Bedeutung für das Zustandekommen der Anfälle und für die therapeutische Bekämpfung derselben. *Z. ges. Neurol. Psychiat.*, 1930, *125:* 475–572.
10. Penfield, W. Meningocerebral adhesions. A histological study of the results of cerebral incision and cranioplasty. *Surg. Gynec. Obstet.*, 1924, *39:* 803–810.
11. Penfield, W. The mechanism of cicatricial contraction in the brain. *Brain*, 1927, *50:* 499–517.

EXTRADURAL CEREBELLAR HEMATOMA. A CASE REPORT*

FRANK TURNBULL, M.D.
Sub-department of Neurology and Neurosurgery, Vancouver General Hospital, Vancouver, B.C.

(Received for publication June 8, 1944)

THE MOST interesting feature of cerebellar extradural hematomata for the neurosurgeon is their rarity. The diagnostic and therapeutic problems arising from this complication of head injury have been mentioned in the literature only during the past decade, and very few case reports have been published. All of the instances of this rare syndrome that have appeared to date have dealt with cases of acute cerebellar extradural hematoma. The following case seems worthy of record as the first account of a patient who suffered from delayed symptoms. Whether it should be described as a subacute, or as a chronic, extradural cerebellar hematoma is a debatable point.

CASE REPORT

Mrs. T.A., age 38, referred by Dr. R. Woodworth of Kimberley, B.C., was admitted to the Vancouver General Hospital on October 19, 1943. She complained of headache, diminished vision in the left eye, and unsteady gait. Her past and family history were not relevant. She led an active life as the mother of five children. Her symptoms commenced in December 1942, when she fell on some ice and suffered a blow across the left eyebrow which caused a deep laceration. She did not lose consciousness. Thereafter she continued to have periodic mild frontal headaches which were troublesome but not incapacitating. On October 6, 1943, nine months after the first injury, while stepping into a car she struck her left forehead forcibly against the edge of the car seat. There was no loss of consciousness and no local bruising. The following morning she noted pronounced blurring of vision in the left eye. During the subsequent week she felt rather drowsy and her headaches became severe. She also noticed slight unsteadiness of her gait. A lumbar puncture was done by her local physician one week after the second injury. He reported that the fluid was clear and initial pressure elevated to 230 mm. water.

Examination. She was a healthy appearing, somewhat obese woman. Urinalysis, red and white cell count were normal, and blood Kahn was negative. Blood pressure 145/90. General physical examination was not remarkable. Neurological examination revealed the following abnormal features: (1) Slight stiffness of the neck. (2) Pronounced choking of the left optic disc with scattered, fresh hemorrhages and exudate around the disc. Vision in this eye restricted to perception of light and gross movements in the left upper quadrant. Mild choking of the right optic disc with normal vision in this eye. (3) Slight incoordination of the right arm and right leg. (4) Diminished tendon reflexes in the right leg. (5) A tendency to stagger to the left when walking.

The evidence favoured a diagnosis of cerebellar tumour but localizing signs were not conclusive. Ventriculography was carried out. The cortex appeared slack through the routine bilateral occipital burr holes. A ventriculogram revealed an internal hydrocephalus of moderate extent. A few bubbles of air were seen to have passed through the aqueduct of Sylvius and lay on the left side of the cisterna magna. There was no evidence of fracture of the skull in the X-ray films.

* Read before The Harvey Cushing Society, New York City, May 17, 1944.

Operation. This was performed (assisted by Capt. P. Lehman, R.C.A.M.C.) on October 23, 1943, nine months after the first head injury and three weeks after the second. The cerebellum was approached by a vertical midline incision. A burr hole over the left cerebellar hemisphere disclosed normal dura; on the right side the burr hole disclosed a hematoma. Bone was removed from over this right cerebellar lobe and the right side of the arch of the foramen magnum. A round, friable clot about the size of a golf ball was uncovered. It lay over the center of this lobe. It was easily removed by suction and no fresh hemorrhage occurred. The margin of the clot was adherent to the dura but could be scraped off. The dura remained depressed. Removal of bone had not been extended out to the margins of the lateral sinus but did reach beyond the margins of the clot. The dura was not opened. The wound was closed tightly leaving a rubber drain leading down through a stab wound to the extradural space.

The drain was removed after 36 hours.

Course. She made an uneventful recovery and left the hospital on November 6, 1943, 14 days after operation. When re-examined on December 15, 1943, six weeks after operation, she complained only of some insomnia and occasional cardiac palpitation. There was no unsteadiness of gait and no evidence of incoordination of the right arm or leg. The outlines of the right optic disc remained slightly blurred with normal vision on this side. The left optic disc was flat and pale; vision for reading on this side was 70 per cent. This unilateral visual disturbance was still present five months after operation, and there was occasional soreness of the involved eye. Otherwise she was in good health.

DISCUSSION

The absence of any similar case reports in the literature may indicate that this case is a freak. There seems to be little need to establish a new clinical syndrome because the history and clinical picture of such a case would lead any neurosurgeon to explore the posterior fossa and apply appropriate treatment. An awareness of this unique lesion will probably enable some neurosurgeon in the future to arrive at the correct diagnosis before exploration.

It is of interest to note that only four cases of uncomplicated acute cerebellar extradural hematomata are on record. Two of these patients survived. In all instances the signs and symptoms of extradural cerebellar hematoma followed a head injury by a few hours or a few days and there was no doubt about the relation of trauma to the clinical picture. The only puzzle was the location of the traumatic pathology within the head.

In 1938 McKenzie[3] discussed 20 cases of extradural hemorrhage and included in this group one case of extradural hemorrhage over the right cerebellar hemisphere. The patient was a child who sustained a slight head injury and after an interval of 30 hours became stuporous. The only abnormal neurological feature was marked flaccidity of all limbs. The child died 14 hours after onset of stupor during a fit which commenced on the right side of the body and was followed by opisthotonos. Necropsy disclosed a short fracture of the occipital bone and a cerebellar clot which was identical in size and position with the clot found in my case.

Coleman and Thomson[1] described the case of a child, age 9, who fell striking the back of the head and was not rendered unconscious. Early observation of the patient disclosed no abnormal neurological signs. Twenty-four hours later he developed some headache and drowsiness but again the

examination was negative. The drowsiness and headache with occasional vomiting persisted until 60 hours after injury. At this time the drowsiness increased, and examination showed stiffness of the neck, hypotonia of all limbs and areflexia. An X-ray film disclosed a long linear fracture in the midline extending into the foramen magnum. At operation a bilateral cerebellar extradural hematoma was removed and the patient recovered. Coleman and Thomson also reported an unpublished case observed by Mayfield. The patient was suspected of having a cerebellar clot but died before operation could be performed. Necropsy revealed an extradural cerebellar hematoma.

Kessel[2] reported the case of a 24 year old girl who fell off her bicycle and struck the back of her head. She was unconscious for a few minutes but shortly after the accident complained only of severe headache. Neurological examination was negative. X-ray films showed a slight separation of the left half of the lambdoid suture. Thirty hours later she suffered a tonic fit which was repeated twice on the following day. A profound coma gradually developed. Lumbar puncture demonstrated a cerebrospinal fluid block. There was no hypotonia and reflexes remained active. Operation disclosed a clot that covered the dura over the left cerebellar hemisphere. The cistern was opened and fluid escaped under considerable pressure. Convalescence was complicated by a cerebrospinal fluid leakage which eventually ceased spontaneously. The patient recovered completely.

There are scattered reports in the literature of acute extradural cerebellar clots which were continuous with clots over the cerebrum. In those cases there had been stripping of the lateral sinus from the bone which provided an added source of bleeding, but the main clot was over the cerebrum. This communication deals only with extradural clots that are limited to the posterior fossa.

In the case which is herein reported the patient suffered two very similar head injuries. One of these injuries occurred nine months and one approximately three weeks before operation. The first injury was moderately severe, the second injury comparatively mild. Headache commenced after the first injury and was only aggravated by the second. The gross loss of vision in one eye, which was produced by choked disc, was apparent the first day after the second injury and signs of cerebellar dysfunction developed thereafter.

Subacute extradural hematomata over the cerebral hemisphere are uncommon, but not rare. Chronic extradural hematomata over the cerebrum, on the other hand, are distinguished by their absence. Presumably the large extradural clots either kill or are cured by operation, while the smaller clots are absorbed so completely that they cause no symptoms. If there is any analogy between extradural clots and traumatic clots found elsewhere in the body, e.g., in the muscles of the thigh, one would expect that, in some instances, absorption of the clot in the extradural space would leave a more or less well-vascularized pseudomembrane. Such a hypothesis is advanced to explain the case that is now reported. The original injury might have

established a vascular pseudomembrane outside the dura and subsequent injury caused re-formation of a gross clot.

Any further inferences do not appear warranted on the basis of a solitary case. It is hoped that publication of this story will serve to unearth other similar accounts, for it surely cannot be as unique as the silent literature would indicate.

REFERENCES

1. Coleman, C. C., and Thomson, J. L. Extradural hemorrhage in the posterior fossa. *Surgery*, 1941, *10:* 985–990.
2. Kessel, F. K. Cerebellar extradural hematoma. *J. Neurol. Psychiat.*, 1942, *5:* 96–100.
3. McKenzie, K. G. Extradural haemorrhage. *Brit. J. Surg.*, 1938, *26:* 346–365.

BILATERAL NERVE DEAFNESS, PERSISTENT COUGH AND PAROXYSMAL HYPERPNEA DUE TO A TUMOR IN THE FLOOR OF THE FOURTH VENTRICLE

DANIEL WELLER, M.D.*
Neurological Service, Lenox Hill Hospital, New York, New York

(Received for publication June 20, 1944)

ATYPICAL cases at times are instructive concerning the physiopathologic mechanisms that come into play as a result of disease or disturbance of certain vital centers. Such cases are of importance in that they confirm or refute accepted physiologic principles based upon observations on animals or normal persons. Because of these facts, the following record is presented.

REPORT OF CASE

A 22-year-old nurse was first admitted to the Lenox Hill Hospital, New York City, on October 20, 1941, because of bilateral deafness. Nine months previously onset of rapid, progressive deafness in the left ear had occurred, and three months later impairment of hearing in the right ear. In addition, for several months she had had frequency of urination and had become fatigued easily. There had been no otorrhea, tinnitus, dizziness, headache or disturbance in equilibrium. The family and past personal histories were noncontributory.

Examination. The patient was ambulatory, afebrile, cooperative and alert. In repose the facial expression was somewhat drawn and blank. The heart and lungs were normal. The ears, nose and throat were essentially negative.

On neurologic examination the fundi and visual fields were normal, as were the other cranial nerves, with the exception of the auditory nerves. Bone and air conduction were poor on both sides. Caloric tests showed active labyrinths bilaterally. The deep reflexes were exaggerated, those on the right side being greater than those on the left. There was transient right ankle clonus. The abdominal reflexes were weak to absent in all four quadrants. There were no pathologic reflexes. There were no motor weaknesses, sensory disturbances or cerebellar signs.

The hemoglobin was 95 per cent; erythrocytes 4,380,000; and leukocytes 9,950, with polymorphonuclears 52, lymphocytes 28 and monocytes 1 per cent. The Wassermann reaction was negative. The creatinine was 0.5, uric acid 3.6, sugar 83, and CO_2 48.1 mg. The spinal fluid examination gave the following results: Initial pressure 80 mm. of water, cells 1, protein 18, glucose 59 and chloride 743 mg.; the Wassermann test and the colloidal gold curve were negative. The basal metabolic rate was +9 per cent.

Course. The patient was discharged on October 30, 1941, no diagnosis having been established.

Second Admission. She was readmitted to the hospital on February 9, 1942, complaining of severe, throbbing frontal headaches, sometimes relieved by lying down. Nausea and vomiting occasionally were associated with these headaches. She believed that the headaches followed the original spinal tap. In addition, she occasionally dropped objects from the right hand. The neurologic status was essentially the same, except for questionable nystagmus on lateral gaze. Lumbar puncture showed an initial pressure of 120 mm. of water, normal dynamics and normal chemistry. Roentgenologic examination of the skull was negative. Ventriculograms were reported as normal. She was discharged on March 1, 1942, without a diagnosis.

---

* Fellow in Neurosurgery, The Lahey Clinic, Boston, Massachusetts.

Interval Note. The patient remained at home and was asymptomatic except for impaired hearing until five weeks later.

Third Admission. When she reentered the hospital on April 22, 1942, she had had severe headaches and vomiting for a week.

The neurologic examination revealed normal fundi, bilateral nerve deafness and occasional nystagmoid jerks on lateral gaze. The deep reflexes were hyperactive, those on the right being greater than those on the left. The abdominal reflexes were absent. There was no Babinski or Hoffmann's sign, motor weakness or spasticity. Light touch, pinprick, position and vibration sensations were diminished over the right arm, trunk and leg.

One week later she began to complain of a difference in the two sides of the body and stiffness of the right arm and hand. The headache became unbearable. The pupils were moderately dilated and reacted sluggishly to light. Well maintained nystagmus was present on lateral gaze. The hemihypesthesia became more pronounced, and the sensory loss involved the right side of the face.

Within 24 hours the patient developed a dry cough, which was resistant to all types of medication. The lungs were clear to auscultation and percussion. Roentgenograms of the chest were negative, and fluoroscopic examination showed normal movement of both leaves of the diaphragm. The dry, rasping character of the cough and its occurrence at regular intervals during an hour, as well as its resistance to medication, suggested central origin. Cocainization of the posterior pharynx and larynx was tried unsuccessfully in an attempt to break the reflex arc, and basal anesthetics were necessary to prevent exhaustion. The cough developed into a peculiar rasping, expulsive shriek. The patient vomited and retched frequently. Since she was unable to take food by mouth, parenteral feedings were begun. She became hoarse, was able to speak only in a whisper, and also began to have periodic tremors of the entire right side of the body. Bronchoscopy failed to reveal the cause of the cough. At the end of the second week in the hospital she complained of weakness on the right side. There was objective evidence of a right hemiparesis with exaggerated reflexes and a right Hoffmann's sign.

Operation. Because of the patient's persistent cough and rapid decline, ventriculograms were again performed, but failed to show any abnormality of the ventricular system. In spite of this, a suboccipital exploration was performed on May 9, eighteen days after admission. Upon opening the posterior cistern, a smooth, bluish, elongated mass was disclosed attached to the posterior aspect of the medulla. This mass extended into and was also attached to the floor of the fourth ventricle, and extended downward to the level of the atlas. It was attached firmly to the cord and was impossible to remove, but some specimens were taken for biopsy. The histologic report was medulloblastoma.

Postoperative Course. As soon as the decompression was accomplished, pronounced improvement in the patient's respiration and general condition occurred. By the following day the paroxysmal cough had disappeared and, except for a right upper monoplegia, she was fairly comfortable. Ten days postoperatively deep radiation therapy to the suboccipital area was started.

The patient ran a stormy course with paroxysms of hyperpnea and apnea, and at times she was cyanotic, cold and clammy. Carbon-dioxide determinations, following a prolonged attack of hyperpnea, revealed a marked acidosis. Intense alkali, blood, glucose and saline infusions restored the blood chemistry to within normal limits, and on about the 28th day she began to improve. The respiratory crises, although of a milder degree, continued until a few days before dismissal on the 49th postoperative day.

The neurologic examination on discharge showed that she was comfortable and free from cough, respiratory crises, vomiting and nausea. The pupils reacted promptly to light and in accommodation, and the fundi were normal. The only persistent signs were the right-sided hemianesthesia and weakness of the right upper extremity.

Interval Note. When seen in the follow-up clinic two months later she was able to walk, and felt well, except for a persistent headache and occasional bouts of respiratory difficulty. The

cranial nerves were essentially negative. She was able to write her name, and the motor power in the right side definitely had improved. However, the right hemianesthesia persisted in all modalities. The operative area was well healed and not bulging.

Fourth Admission. The patient returned to the hospital on October 21, 1942 for further radiation therapy. The neurologic status was essentially the same. Her facies was pale and gave the impression of chronic ill health. After every radiation treatment she had a respiratory crisis characterized as follows: Within a few hours she began to breathe rapidly. The respirations were shallow, often simulating the panting of a dog, and varied from 60 to 112 a minute. The breathing was so labored that each inspiration and expiration was attended by a simultaneous lateral propulsion of the head as the accessory muscles of respiration came into play. This hyperpneic phase, which lasted from a few hours to as long as forty hours, then subsided until the respirations were down to 8 to 10 a minute. During this apneic phase, which often persisted for as long as sixteen hours, she was comatose.

Roentgenologic examination of the chest on October 23 revealed changes simulating a pneumonitis, although physical examination failed to disclose any positive signs of involvement of the lung, and the patient's temperature was normal. Because of the respiratory embarrassment, which apparently was due to radiation therapy, smaller doses were attempted but were not tolerated. There was no change in the neurologic status. Roentgenologic examination of the lungs three weeks after admission was essentially the same as on admission. The patient was discharged on November 22, 1942, to the care of her family physician, and further information concerning her course is not available.

DISCUSSION

Although tumors of the fourth ventricle do not produce a typical clinical syndrome, they seldom present such a misleading sign as bilateral deafness. In most instances, regardless of the initiating symptoms, signs of increased intracranial pressure, with or without involvement of the pons, medulla or cerebellum, appear. Craig and Kernohan[2] list headache, choked disk, vomiting, ataxia, diplopia, stiff neck and hiccup as predominant in their series of 82 cases. All these symptoms result from either obstruction to the cerebrospinal fluid circulation or direct local involvement of the medulla by the tumor mass itself.

Bilateral nerve deafness, central cough and paroxysmal hyperpnea, without signs of increased intracranial pressure, were the outstanding features in this case. In order fully to appreciate this bizarre picture, one need only recall the compactness of the vital centers and the numerous structures in the floor of the fourth ventricle. In addition to the three important vagal, hypoglossal and acoustic trigones, there are the three cerebellar peduncles, and the nucleus of the sixth nerve (eminentia teres). Adjacent and posteriorly are the expanded parts of the posterior columns named the clavus and cuneus.

Regardless of our knowledge of the anatomic arrangement in this area, the neurophysiologic mechanisms involved are difficult to understand. Brain tumors, other than cerebellopontine angle tumors, do not play an important part in nerve deafness, although it does occur with midbrain lesions,[6] usually late in the course of the disease. Studies by Craig and Kernohan,[2] Gibbs,[4] Drury[3] and Northington[5] fail to mention examples of fourth ventricle tumors as a cause of such deafness, although the position of the acoustic apparatus

in the floor of the fourth ventricle is so superficial as to be vulnerable. Nevertheless, deafness may occur late in chronic, focal pressure on the brain stem, but in these instances it is usually unilateral.

The respiratory and coughing mechanisms are regulated by centers located in the lower part of the medulla, primarily from impulses along the vagus nerve and tractus solitarius.[1] Under normal conditions they respond to variations in the carbon-dioxide content of the circulating blood and stimuli from the respiratory mucosa, as well as impulses set up by the expanding and contracting lung. Theoretically, it is remarkable that disturbances of respiration, such as were present in this case, are not more frequent in cases of fourth ventricle tumors, although they have been noted in cases of encephalitis with acute bulbar symptoms.[7] Usually one encounters the Cheyne-Stokes type due to tonsillar herniation.

In the case reported the breathing was of the Biot type, in which the onset of hyperpnea and apnea is paroxysmal. As a result of this anoxia, the patient was cold, cyanotic and lightheaded. Continued hyperpnea induced an acapnea, and during this phase the patient's respiration frequently was decreased below 8 a minute. Contrary to experimental findings,[1] there was no consistent correlation between the hyperpneic phase and the pulse rate and blood pressure. The blood pressure was maintained on a steady level. At times the pulse rate was increased and at other times it was unchanged.

The secondary lung changes consequent to the protracted hyperpnea, which undoubtedly were due to vascular changes in the parenchyma of the lung, were most interesting. The nature of the lesion and the slow progression of the changes in the lung, as shown by roentgenologic examination, were not characteristic of metastasis but rather of a pneumonitis.

The neurologic signs pointed to direct involvement of the posterior columns, the pyramidal tract and the spinothalamic pathways. The true nature of the lesion was not suspected until these structures became involved.

SUMMARY

A case is reported of a tumor of the fourth ventricle which manifested itself by signs of an unusual disturbance in the respiratory centers, together with deafness. Tract signs were not produced until late in the course of the disease. The disturbance in the respiratory center produced paroxysms of the Biot type of breathing and periods of uncontrollable coughing. The changes in the parenchyma of the lung were secondarily induced, probably based upon alterations in the blood vessels of the lung.

The author wishes to express his gratitude to Dr. T. K. Davis, Director of the Neurological Service, Lenox Hill Hospital, New York City, for his assistance and his permission to present this case; also to Dr. Gilbert Horrax, Director of the Department of Neurosurgery, Lahey Clinic, Boston, for his many helpful suggestions.

REFERENCES

1. Best, C. H., and Taylor, N. B. The physiological basis of medical practice. *Baltimore: Williams & Wilkins Co.*, 1943, 3rd ed., 1942 pp.
2. Craig, W. M., and Kernohan, J. W. Tumors of the fourth ventricle. *J. Amer. med. Ass.*, 1938, *111:* 2370–2376.
3. Drury, D. W. Aural acuity and brain lesions. 1—Audiometric studies. *Trans. Amer. Otol. Soc.*, 1931, *21:* 221–249.
4. Gibbs, F. A. Frequency with which tumors in various parts of the brain produce certain symptoms. *Arch. Neurol. Psychiat., Chicago*, 1932, *28:* 969–989.
5. Northington, P. The hearing in patients with intracranial tumors. Report of fifty-two cases. *Bull. neurol. Inst., N. Y.*, 1936, *5:* 289–303.
6. Sloane, P., Persky, A., and Saltzman, M. Midbrain deafness. Tumor of the midbrain producing sudden and complete deafness. *Arch. Neurol. Psychiat., Chicago*, 1943, *49:* 237–243.
7. Wilson, S. A. K. Neurology. *Baltimore: Williams and Wilkins Co.*, 1940 (p. 120).

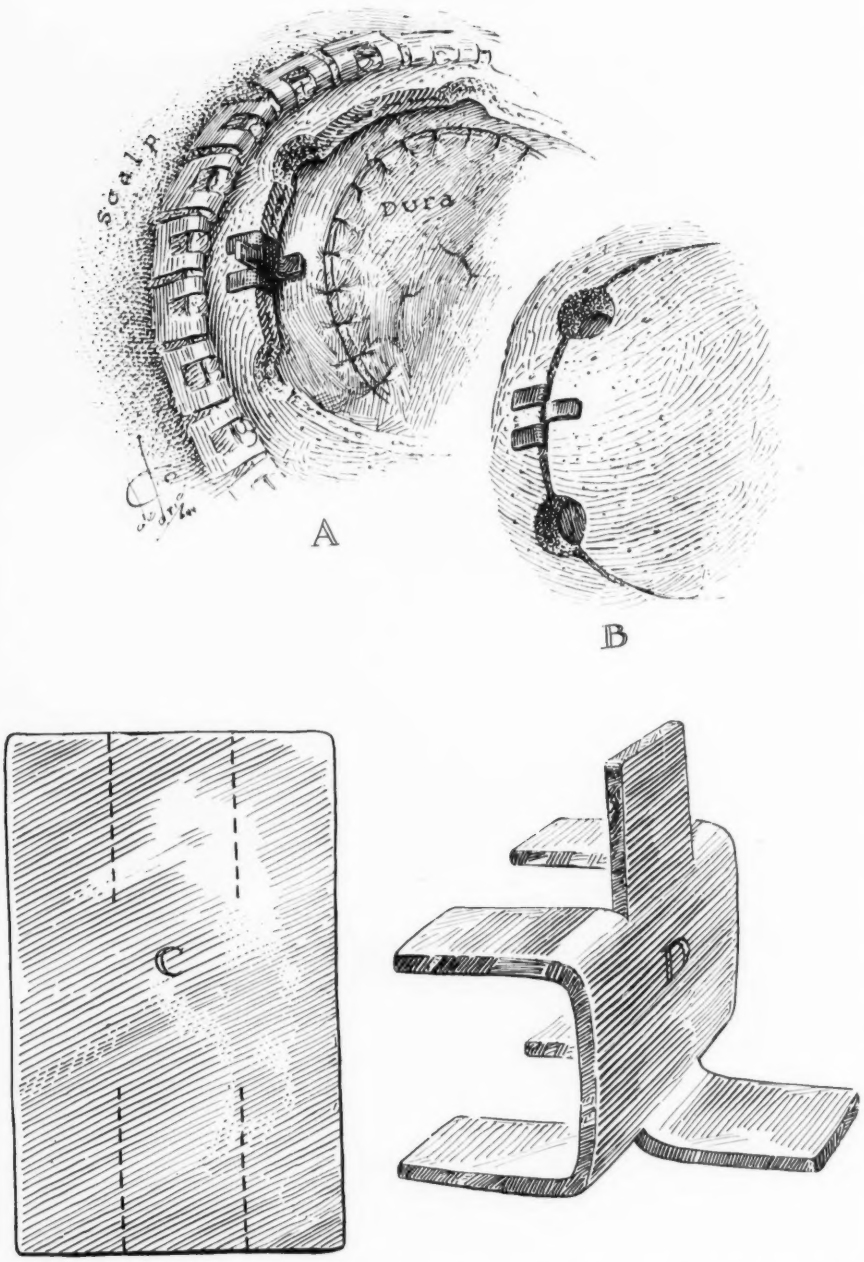


FIG. 1. *A* Tantalum clip applied to edge of bone with one prong left vertical. *B* The bone flap in place and the clip bent upon it. *C* Pattern for cutting clip from .020-inch tantalum plate. *D* The formation of the clip.

A TANTALUM CRANIAL CLIP

WALLACE B. HAMBY, M.D.
Buffalo General Hospital, Buffalo, New York

(Received for publication June 28, 1944)

THE USE OF the beveled Gigli saw-cut in performing a craniotomy allows replacement of the flap with a minimum of deformity. In the average case no mechanical restraint of the flap is necessary since closure of the overlying tissues fixes it securely. In some instances, however, the flap must be wired into place. If the lower end of a frontal flap be cut with a DeVilbiss rongeur the resulting defect often is wide enough to produce an unsightly ridge. Wiring usually does not prevent depression of such a flap.

A simple clip to prevent depression of the bone flap has been used recently in a few cases. The clip is cut with tin snips from .020-inch sheet tantalum. Only small squares (2 cm.) are necessary, and the residual tantalum left after fashioning a plate for cranioplasty will suffice for several. In Fig. 1 the formation and application of the clip are explained. A large hemostat or bone-holding forcep is useful for clamping the clip on the edge of the skull. The bone flap then is replaced and the vertical portion of the clip is bent down upon it. One clip may be sufficient; others may be used if necessary.

OPERATIVE RESULTS IN INTERVERTEBRAL DISCS*

FRANCIS C. GRANT, M.D.
Department of Neurologic Surgery, Philadelphia General Hospital, Philadelphia, Pennsylvania

(Received for publication July 22, 1944)

THAT PAIN in the back and along the sciatic nerve, known to our forebears as sciatica, can be caused by rupture of an adjacent intervertebral disc has introduced a tangible factor into the hitherto uncertain etiology of this distressing condition. Furthermore, the removal of the ruptured disc by a simple operative procedure has been widely heralded as the most certain method of relieving this pain. Prior to 1930, a sufferer from low back pain with sciatica remained in bed until his pain disappeared. Heat, elimination of foci of infection, traction on the leg, and injection of the nerve trunk with saline solution, were all used in an attempt to secure relief, but the basis of treatment was rest. The patient was more comfortable in bed and so he stayed there. All of these patients recovered more or less after a longer or shorter rest and were able to be up and about under certain handicaps. They wore braces to protect and support their backs and they changed from one type of work to another which put less strain on the back muscles. In general, they did not do so badly.

The discovery of the ruptured disc and its relation to low back pain and sciatica has introduced surgical removal of the disc as a method of treatment. Many papers have been written on this subject; the diagnostic criteria are now well established, and the operative technique is standardized. However, more emphasis has been laid upon these two points than upon follow-up statistics. A ruptured disc causing low back and sciatic pain may produce more or less intense discomfort to the patient, but the condition never of itself resulted fatally. To advise surgery in a situation of this kind, even when the surgery is as relatively safe and simple as is that demanded in the removal of a ruptured disc, places considerable responsibility on the surgeon. With even the simplest and easiest surgery unfortunate accidents can and have occurred. The decision to operate is, therefore, based on its expediency. Following operative removal, will the patient be relieved of his discomfort so that he can return to work? What are the chances of no relief of pain or of increase of disability following surgery? It is high time that more emphasis be laid upon operative results than upon diagnostic methods and surgical technique.

This paper has to do solely with operative results as indicated by post-operative examination of the patients at periods ranging from five years to six months. But two reports, by Verbrugghen[2] and Shinners and Hamby[1], have been found which deal solely with the condition of the patient following

* Read before The Harvey Cushing Society, May 18, 1944.

removal of the disc. All the other communications we have found have given methods of diagnosis and operative technique in large groups of patients, but have been noticeably vague about end results. Frankly, we have not been overly enthusiastic about the final consequences of this surgical procedure. Too much has been said about the ease of diagnosis and surgical technique and too little about the state of the patient afterwards. It is interesting to note how closely our figures coincide with Hamby's, while Verbrugghen's statistics draw a very somber note as far as end results are concerned.

Pain produced by a ruptured disc has two components, the pain in the back and the pain in the leg. Back pain is the initial complaint followed by pain radiating down one leg. Leg pain in the sciatic distribution leads to the suspicion or certainty of a ruptured disc. Pain in the back is due to pressure on, or rupture of, the posterior vertebral ligaments. Pain down the leg is caused by the protrusion of the disc against the adjacent lumbar nerve roots. These two pains are different components of the same progressive picture, and both are important in its recognition. Why does the disc rupture? Trauma, a twisting wrench of the lumbar vertebra, is a commonplace finding in many histories. But in other instances, a no more serious injury than rolling out of bed has been noted. Does the disc rupture because of some structural disability of the back and is the low back pain the earliest clinical evidence of such weakness? This point, I believe, is very important, because, while by the removal of the disc the leg pain is almost always relieved, the pain in the back may remain and produce discomfort and disability.

It is necessary to state here that, while we are convinced that these two pain components exist and for different reasons, as outlined, we have had no experience with fusion as a means for relief of the back pain following improvement or relief of the leg pain by removal of the disc. It is hoped that the indications for and results of fusion will be one of the points brought out in the discussion.

One hundred and fifty cases of ruptured intervertebral disc verified at operation form the basis of this report. All of these patients were operated upon prior to December 1, 1943, thus allowing at least a six months' follow-up period. One hundred and twenty-six of these patients were recently seen and examined. In twenty-four instances, what were considered adequate replies were received to a questionnaire. Interest centered in only one group of facts: what was the patient's condition before operation and how was he affected by operative intervention. When first seen, 11 patients were bedridden, 27 were unable to do gainful work of any kind, and 112 were working with disabilities. The average length of time between the first attack of pain and operation was $2\frac{1}{4}$ years. One hundred and twenty-one patients had had two or more attacks of back and leg pain prior to operation.

At present, 78 of these 150 patients are completely cured and are back at work with no disability whatsoever. In this group of 150 cases, 71 patients were employed at what has been termed hard labor: mining, farming, shipbuilding, nursing. Of these 71 patients 34, or 48 per cent, are entirely free

from any pain whatsoever in either back or leg and have returned to their jobs without any disability; 28, or 41 per cent, have had some back pain or numbness in the leg on the operated side. They are working at their previous tasks under some disability or have changed to lighter work. Nine patients, or 11 per cent, were entirely unrelieved following operation.

Seventy-nine patients fall into the non-laborer group: clerks, executives, professional men, housewives. Forty-four, or 55 per cent, are back at work without disability; 28, or 35 per cent, are carrying on with some back pain although glad they were operated upon; and 7, or 10 per cent, are unimproved.

Considering now the degree of preoperative disability and the postoperative results, of the 11 bed-ridden patients, 6 are back at their previous jobs, 4 laborers and 2 non-laborers; 3 are employed in less arduous labor and doing well; 2 are unable to do any work. Among the 27 unable to work preoperatively, 12 laborers and 5 non-laborers are back at work; 6, 3 laborers and 3 non-laborers, are improved; and 4, 3 laborers and 1 non-laborer, are unimproved. Of the 117 patients working with disability, 55 are cured, 47 are improved, and 10 not improved, following surgical intervention.

These last figures seem to confirm the impression gained from clinical experience that the greater the amount of preoperative pain, the better the final result. It is also interesting to note that of the 16 failures, 8 had had but one attack of pain prior to operation. At present, no patient suspected of having a ruptured disc is considered for operation unless he has had two attacks or more of pain and unless the pain is severe at the time he presents himself in clinic. To operate upon a patient who has had his attack and whose pain is definitely receding is unwise. All these persons will have some distress for a longer or shorter period postoperatively. If they have had a great deal of pain preoperatively, this postoperative readjustment period means little to them. Their major pain is relieved and the mild postoperative pain is readily accepted. But if the preoperative pain is mild, particularly if the surgeon has been unwise enough to promise complete relief, then this postoperative pain discourages them; they feel the operation has been a failure and the final result is much less satisfactory.

In the course of the review of the material on which this paper is based, the histories of 93 patients were found in whom, either on clinical grounds alone (60 cases) or on the basis of the clinical findings plus the use of intraspinal contrast medium studies (33 cases), the diagnosis of ruptured disc seemed certain; as assured, at least, as any of the operated group. For various reasons these patients were treated conservatively. All were seen prior to January 1, 1943, so that a year or more follow-up is available. Fifteen were bedridden; 9 of these have completely recovered and are back at their original work. Six of these patients were housewives, 3 were clerks. Three have improved enough to carry on light work around a farm. Forty-two were unable to work. Thirty-six have recovered sufficiently to return to less

arduous work, 6 are still not working. Thirty-six were working with disabilities and are still at work, although 24 of them have had to change the type of their employment.

It is admitted, of course, that in any of the patients in this non-operated group, a recurrence or severe increase of pain can occur at any time, if they are unlucky enough to twist their backs in such a way that the disc will protrude again. Operation may then be done. Furthermore, this is a relatively small group of cases. Nevertheless it is worth noting that they have made progress under conservative treatment alone.

Following this assessment of our results with the surgical treatment of ruptured discs, we see no reason to change the conservative attitude we have adopted in the past two years. Surgery is not, in our opinion, the only treatment for this condition. The question as to whether surgery is expedient should always be considered. Many of these patients will recover with rest, leg traction, back support, and other non-operative means. If this is unsuccessful, or if a severe recurrence of pain is noted, surgery should be considered. Nature will care for many of these sufferers, exactly as was the case prior to 1930. It seems presumptuous of the surgeon to interfere until after he has given Nature every chance. The results from surgical treatment do not seem sufficiently good to warrant it.

TABLE I. *Ruptured discs verified by operation.*

Total number of cases			150
Six months' follow-up records			
Laborers	71	Non-Laborers	79
Men	87	Women	63
Operations			159
Mortality			0
Laborers			
Working with Disability			51
Unable to Work			15
Bedridden			5
Non-Laborers			
Working with Disability			61
Unable to Work			12
Bedridden			6

TABLE II. *Results of operation.*

Cases	150
Back at Work—No Pain	78–52%
Working with Disability	56–37%
Not Working	16–11%

TABLE III. *Labor group.*

Cases			71
Men	59	Women	12
Working with Disability			51
Unable to Work			15
Bedridden			5

Operative Results

Back at Work—No Disability	34—48%
Back at Work—with Disability or Change of Job	28—41%
Unimproved	9—11%

TABLE IV. *Non-labor group.*

Cases			79
Men	28	Women	51
Working with Disability			66
Unable to Work			8
Bedridden			5

Operative Results

Back at Work—No Disability	44—55%
Back at Work—with Disability or Change of Job	28—35%
Unimproved	7—10%

TABLE V. *Disc—ruptured through annulus.*

Cases	46

Laborers		Non-Laborers	
Cured	7	Cured	14
Improved	11	Improved	11
Not Improved	1	Not Improved	2

Cured	21—45%
Improved	22—48%
Not Improved	3— 7%

TABLE VI. *Disc—protruded through annulus.*

Cases	74

Laborers		Non-Laborers	
Cured	20	Cured	27
Improved	10	Improved	12
Not Improved	3	Not Improved	2

Cured	47—63%
Improved	22—30%
Not Improved	5— 7%

TABLE VII. *Disc—hidden and curetted.*

Cases			30
Laborers		Non-Laborers	
Cured	7	Cured	3
Improved	7	Improved	5
Not Improved	5	Not Improved	3
Cured			10—33%
Improved			12—40%
Not Improved			8—27%

TABLE VIII. *Conservative treatment.*

Cases		93
Bedridden	15	
Complete Recovery		9
Partial Recovery		3
Unimproved		3
Unable to Work	42	
Complete Recovery		12
Partial Recovery		24
Unimproved		6
Working with Disability	36	
Changed Job		24
Same Job		12

TABLE IX. *Summary of operative results.*

Bedridden	11	Cured	6	Improved	3	Not Improved	2
Unable to Work	27	Cured	17	Improved	6	Not Improved	4
Working with Disability	112	Cured	55	Improved	47	Not Improved	10
	150		78		56		16

REFERENCES

1. Shinners, B. M., and Hamby, W. B. The results of surgical removal of protruded lumbar intervertebral discs. *J. Neurosurg.*, 1944, *1:* 117–122.
2. Verbrugghen, A. H. Herniated nucleus pulposus. A report of 75 cases examined and operated. *Dis. nerv. Syst.*, 1943, *4:* 165–177.

TRANSACTIONS OF THE HARVEY CUSHING SOCIETY
THIRTEENTH ANNUAL MEETING
HELD AT THE COMMODORE, NEW YORK CITY
MAY 17 and 18, 1944

EDGAR F. FINCHER, M.D., *President, in the Chair*

May 17, 1944

THE TREATMENT OF HYPERSENSITIVE CAROTID SINUS BY GLOSSOPHARYNGEAL NERVE SECTION

Dr. Bronson S. Ray and Dr. Harold J. Stewart (by invitation).

This paper presents a report of two cases in which section of the glossopharyngeal nerve intracranially has controlled fainting attacks due to carotid sinus syndrome. It discusses in general the role of the glossopharyngeal nerve in the carotid sinus reflex.

DISCUSSION

Dr. Harold J. Stewart: There is one point we would like to make in addition to what Dr. Ray has said. We have not been completely content with the grouping which Weiss and his coworkers made of the sensitive carotid sinus. He, as you recall, recognized three types of sensitivity: the vagal type, the depressor type and the cerebral type. Most patients we have seen belong to the vagal type, in the reproduction of whose attacks were associated marked slowing of the heart with varying periods of asystole, fall in blood pressure and changes in the cardiac rhythm. With reference to this last case in which Dr. Ray showed the electrocardiograms, on one occasion during the test we found that pressure on the side on which the ninth nerve had been sectioned gave a fall in blood pressure. After making many tests we came to the conclusion that if we occluded the carotid artery there occurred a fall in blood pressure, but if we massaged the area without occluding the vessel fall in blood pressure did not occur. The depressor type might be attributed to changes associated with closure of the carotid vessels on that side and not to the sensitive carotid sinus.

Captain James C. White (U.S.N.R.): I think Dr. Ray deserves a great deal of credit for the skill and ingenuity he has used in carrying out this anatomical investigation of the carotid sinus innervation. He should not imply, however, that intracranial section is the procedure of choice. I have done the operation in the neck, particularly for people with convulsive seizures. The anatomy of the plexus is a pretty complicated affair. Its resection is greatly simplified by cutting the external carotid artery where it joins the carotid; this opens up the intercarotid area and facilitates exposure of the plexus. You can then denervate the internal carotid very effectively. I am nearly certain that no recurrences have taken place in these patients. I have followed one case four years.

Dr. Paul C. Bucy: I agree with Dr. White. There are three nerves supplying the carotid sinus. Code and Dingle showed, at least to my satisfaction, that in the dog the carotid sinus nerve is a branch of the ninth nerve while the vagus and sympathetic nerves have nothing to do with the pressor mechanism. These experiments by Dr. Ray are most interesting but I would suggest another possible explanation of the changes that occur following procainization on the side deprived of ninth nerve innervation. This extensive procaine infiltration in the carotid sinus region may interrupt the aortic mechanism as well as the carotid sinus nerve and the rise in blood pressure following injection of novocaine may be due to that rather than to interruption of some carotid sinus fibers derived from some source other than the glossopharyngeal nerve.

DR. JAMES L. POPPEN: I think this is an excellent paper. It certainly gives us new light on different methods of treatment of the hypersensitive sinus. We must be cautious, however, about drawing conclusions. It is important that one does not completely occlude the artery by pressure but massages it gently in order to determine whether it is sensitive. In Dr. Ray's cases were convulsions or syncope produced? When the artery was completely occluded did the patient have convulsions?

We have found infiltration of procaine around the carotid bulb before manipulating or injecting the carotid artery in angiography important to prevent untoward symptoms.

Lastly, from the practical standpoint, most patients can be treated by conservative measures. If after adequate conservative measures there is no improvement, then operation is indicated.

DR. BRONSON S. RAY: Since our interest has been directed toward trying to pick out the function of the ninth nerve in the carotid sinus reflex we have stressed intracranial section rather than operation in the neck. I agree with Captain White that denervation by the neck operation attains satisfactory results in abolishing the reflex, but since all nerve connections are divided by this procedure it would be impossible to draw the conclusions regarding the role of the ninth nerve alone that we have been able to do by the intracranial operation.

I think Dr. Bucy's criticism concerning the interruption of aortic impulses by procaine block of the carotid sinus region is an apt one. However, in some animals the aortic bodies do not exist at all, as in rabbits and rats. Thus, there is a species difference and we still have to determine whether aortic bodies are functional or not in man.

As to the question of convulsions developing in the carotid sinus reflex, I have never been entirely satisfied because it seems to me if one persists in the stimulation long enough, convulsions are likely to develop. My attitude has been that convulsions probably occur as the result of prolonged asystole and drop in blood pressure. I am not convinced there is such a thing as a cerebral type of response without cardiovascular changes in the carotid sinus reflex. I may be wrong, but that is my impression from our work. We have had the experience of finding that convulsions that occurred on pressure on the carotid sinus still occurred after novocainization of that sinus, indicating that they resulted from impairment of the blood supply to the brain.

As to the neck operation, it still holds that intracranial division of the ninth nerve has advantages when it may be undesirable or impossible to perform a dissection in the neck. At the New York Memorial Hospital there are patients who have had considerable trouble from hypersensitive carotid sinuses, first from malignancy in the neck and more often after the malignancies have been treated with roentgenotherapy. One certainly can't advise dissection in the neck in such patients, but if it becomes desirable to relieve a hypersensitive sinus reflex in them we have recourse to the alternative operation of intracranial section of the ninth nerve.

MICROCEPHALUS SECONDARY TO BIRTH TRAUMA

DR. EDGAR F. FINCHER

This paper was published in the July 1944 issue of the *Journal*, page 265.

DISCUSSION

DR. FRANC D. INGRAHAM: I am delighted to know that Dr. Fincher is interested in these patients because there are so many of them and they ordinarily receive all too little attention. It seems to me that the patients he has presented could be divided into three groups: (1) those with cerebral damage at birth; (2) those with premature closure of the sutures who should obviously have craniectomies; and (3) those with definite subdural membranes. It was not

quite clear to me how many of the patients had subdural membranes. I would expect them to be the ones who ran the most favorable course. Ordinarily subdural taps and pneumoencephalograms should serve to differentiate the doubtful cases. If there is any question, burr holes should certainly be done. I would like to know whether Dr. Fincher has opened the dura widely from the temporal region to the midline in the patients who had craniectomies performed. To date, we have been unwilling to open the dura beyond the limits of the area protected by muscle.

Dr. Albert S. Crawford: I would like to ask Dr. Fincher how much bone he takes away. Does he remove a piece of dura or just leave it unsewed so as to make it possible to expand later?

Dr. Edgar F. Fincher: There were 17 cases in the whole group. Five of these were trephine exposures showing no gross extracortical pathology. Of the 12 remaining ones, four were opened unilaterally and the external hydrocephalus was such that we didn't feel even a trephine on the other side would contribute anything. The other eight had bilateral membranes. As to Dr. Crawford's question, the sacrifice has been both dural and membranous, as extensively as a 2½ to 3 cm. exposure would permit. If the arachnoid is not ruptured during the operation, I don't think we have noted any ill effects from leaving the dura wide open. In the child shown with the bulging decompression, aspiration resulted in a goodly escape of fluid from beneath the scalp; it was some weeks before the bulge receded. This might give a false impression of bulging cortex. The others haven't had extensive collections of fluid. We haven't sectioned the longitudinal sinus in any case but carried the incision right up to it and tried not to molest the cerebral veins entering the sinus.

A ROENTGEN STUDY OF THE SUBDURAL SPACE. OBSERVATIONS ON THE PRESENCE OF SUBDURAL GAS FOLLOWING PNEUMOENCEPHALOGRAPHY

Dr. T. C. Erickson and Dr. L. W. Paul (by invitation)

In the attempt to elucidate the mechanism of filling of the subdural space and its possible diagnostic significance a systematic study of the filling of the subdural space is made following routine pneumoencephalograms and on films taken 24 hours later. Subdural filling under the tentorium and the basal cisterns always occurs as a result of direct introduction of gas into the spinal subdural space whence it may also pass to the subdural space over the cerebral hemispheres. Under these circumstances it is obviously an artifact of technique and is of no diagnostic significance *per se*. However, routine study of second-day films as well as of immediate encephalographic films enables one to distinguish in many cases between this artifact and the indirect subdural filling that occurs as a result of laceration of the arachnoid membrane. Presence of subdural gas under the latter circumstances may support a diagnosis of a post-traumatic lesion or other pathologic process producing adhesions between arachnoid and dura but is not pathognomonic of such a condition.

The presence of subdural gas has no apparent relation to the degree of subarachnoid filling on the first day. On the other hand subdural filling is greatest in those cases showing the greatest decrease in size of the ventricles on the second as compared to the first day. Ventricular collapse is an impor-

tant factor in promoting filling of the subdural space. The ventricular size and filling are usually decreased on the second-day films but not infrequently an actual increase is observed and the possible explanations of this finding are discussed. Films taken on the second day after encephalography are also of value because the shifting of air from one ventricle to the other or in the subarachnoid or subdural space enables one to judge more accurately the significance of small differences of filling of various structures. Rarely ventricular filling occurs on the second day when it did not occur on the first day. Certain pathologic structures, notably porencephalic cysts, are often visualized on the second day where their presence is not suspected on the first-day films.

DISCUSSION

Dr. Carl F. List: Introduction of air into the subdural space has been purposely performed in our clinic for two reasons: (1) As a diagnostic method to demonstrate roentgenographically cortico-meningeal adhesions. (2) As a therapeutic procedure to break up such adhesions or to prevent their reformation in certain cases of post-traumatic headaches and convulsions. The number of our patients thus treated is still too small and the observation period too short to evaluate the therapeutic results, but in a few instances there was striking improvement of headache and cessation of convulsive attacks.

[Lantern slides of three cases were demonstrated in which subdural air injection had been carried out both for diagnostic and therapeutic purposes.]

Dr. Paul C. Bucy: I have seen some evidence that leads me to believe that massive accumulation of gas in the subdural space may not be without danger and on occasion may cause a venous tear resulting in subdural bleeding. I wonder if the fluid levels seen in the subdural spaces might be blood rather than cerebrospinal fluid. In my own practice we have limited the maximum amount of fluid withdrawn at encephalography to 150 cc. in any case. Also we have felt oxygen is much more quickly absorbed than air and that its use might lessen the danger of such complications.

Dr. Robert B. Aird: The type of gas employed in pneumoencephalography makes a definite difference in the incidence of subdural gas collections as reported by Drs. Erickson and Paul. Drs. Stone and Jones in 1933 made a splendid study along these same lines. They employed air, made follow-up films at 24 hours as well as at later periods, and showed sagging of the cerebral hemispheres of even more marked and striking degree than that just shown. I have used oxygen in approximately 200 cases and our follow-up studies, which have been made routinely since 1933, show essentially the same results as reported here. In addition, we have about 1,100 cases in which ethylene gas was injected. This gas is absorbed much more quickly than oxygen and correspondingly we have found that the post-encephalographic reactions have been foreshortened and lessened. Approximately 90 per cent of the ethylene disappeared within six hours. With ethylene we have rarely encountered subdural collections and, when observed, they almost invariably appeared early, which makes us feel that they are due to a faulty injection technique, as occasionally may happen if the needles are slightly displaced, and not due to a tear in the arachnoid occurring after the injection is completed, as is presumably the case if the subdural collection is first visualized in the final films of the X-ray study or, more commonly still, in the follow-up films. In our opinion the incidence of subdural gas collections occurring with pneumoencephalography varies widely depending upon the gas used.

Dr. T. C. Erickson: In answer to Dr. Bucy's question that in some cases the fluid level

might represent subdural bleeding, I can say that in some of these cases a burr hole has been made with the finding of clear and colorless or slightly yellowish fluid. This is most frequent in patients with cerebral atrophy and no doubt represents subarachnoid fluid increased *ex vacuo* which has passed along with the gas into the subdural space through a vent in the arachnoid membrane. In contrast to such a secondary subdural effusion there may of course in some cases be a primary subdural effusion. I have seen no case in which there was evidence of subdural bleeding secondary to the pneumogram although it is possible that in rare instances it might occur.

STUDIES ON FIBRIN FOAM AS A HEMOSTATIC AGENT IN NEUROSURGERY, WITH SPECIAL REFERENCE TO ITS COMPARISON WITH MUSCLE

Dr. Franc D. Ingraham, Dr. Orville T. Bailey (by invitation), and
Dr. Frank E. Nulsen (by invitation)

This paper was published in the May 1944 issue of the *Journal*, page 171.

DISCUSSION

Dr. James L. Poppen: Dr. Horrax and I have also used fibrin foam in a number of cases as a result of the generosity of Drs. Ingraham and Bailey. We can say it is certainly far superior to muscle, and as efficacious as the electrosurgical unit. Drs. Ingraham and Bailey gave a very modest presentation. If I had had anything to do with the development of fibrin foam I would think my name one of the outstanding names in neurosurgery.

Fibrin foam is particularly useful in the control of venous bleeding around the sagittal sinus. It is of great help in the pituitary fossa when there is oozing from the cavity after partial removal of an adenoma. I have not found it to be highly useful in the larger tumor cavities because most bleeding in such cavities completely stops when arteries have been coagulated or clipped and the tumor entirely extirpated. It is of aid, also, in a tic operation, particularly in saving time by controlling troublesome dural sinus bleeding. I heartily endorse it as a useful adjunct in control of bleeding.

Dr. William V. Cone: I can testify to the value of fibrin foam and thrombin. I have used it with great success when one of the dural veins was torn at the sinus level and bleeding was difficult to control by muscle. We were able to deal with a situation that might well have been fatal.

Dr. Ernest Sachs: I thoroughly agree with everything that Drs. Ingraham and Bailey have said about fibrin foam. I have lined the wall of a tumor bed with thin sheets of fibrin foam and made it adherent by pressing hot cotton against it. This has worked much more rapidly and more effectively than when we used muscle for the same purpose. I have also used the fibrin foam in a patient with a parasagittal meningioma in whom I had to excise the longitudinal sinus. I controlled the bleeding from the sinus by plastering some fibrin foam over the opening and this became promptly adherent and stopped all bleeding. I have had no occasion to use it on the dura because oozing from the dura is very simply controlled, as a rule, with electric coagulation. I consider the introduction of fibrin foam one of the greatest advances in neurosurgery in recent years.

Dr. Bronson S. Ray: I too have found that fibrin foam does everything others have said it does. Because it is so efficient one may be tempted to expect too much. Recently after I had labored over radical removal of an acoustic neurinoma, troublesome bleeding developed from the pons and was not quickly controlled with muscle stamps. I packed in several large pieces of fibrin foam and all bleeding stopped but as I started closure of the wound, the

whole cerebellum came up out of the fossa. When I looked back I found the foam had been sealing off the whole angle thereby preventing egress of the blood collecting behind it. This was my fault but it demonstrates what may happen if one does not employ the foam intelligently.

MAJOR FRANK H. MAYFIELD: Fibrin foam obviously needs no further endorsement. It will perhaps be of interest to the authors to know that we have used it in one instance in a hemophiliac requiring amputation. Several previous operations had necessitated numerous transfusions and were associated with severe and profound shock. The operation in this instance was done under tourniquet, and thin layers of fibrin foam immersed in thrombin solution were placed between the fascial layers at the time of closure. I am informed by my orthopedic colleagues, to whom I reluctantly gave the material, that there was no bleeding with release of the tourniquet and that healing was as satisfactory as in any plastic revision they have had.

MAJOR BARNES WOODHALL: Lt. Col. Spurling and others of us at the Walter Reed Hospital have used fibrin foam in about 200 cases. It is difficult to say too much in praise of it. It is very bad form for one Army officer to take anything from another but recently I have had to lock up my supply.

I should like to point out some of its applications in military neurosurgery. We have had a good many gunshot wounds of the head, evacuated for reparative neurosurgery. In the repair of the resulting skull defect, fibrin foam has been a most effective agent in the control of diffuse hemorrhage from dural and cerebral scar resections. Its potential value in acute war injuries to the brain is illustrated by a recent experience. A soldier sustained a bilateral frontal lobe injury while welding a large drum. Gasoline fumes exploded and a fragment of the drum lacerated the inferior surfaces of both frontal lobes. The injury was a formidable one but its repair was facilitated greatly by the use of fibrin foam. I am afraid that in the future our young surgeons will forget other methods of hemostasis.

Some tumors operated upon overseas have been returned for completion of the job. Recently an acoustic neurinoma was resected with troublesome bleeding from the border of the pons but the problem of hemostasis was simplified by the use of foam. I am sure that, in the past, I have injured the pons in controlling such bleeding. I can say that in none of our cases has hemorrhage occurred after the use of fibrin foam. In military neurosurgery this would minimize the danger of infection, which may have its source in hematomas.

In peripheral nerve surgery I think we have shown at Walter Reed that bleeding can be controlled with fibrin foam both from epineural sources and from transected nerves prepared for nerve suture or grafting.

DR. FRANC D. INGRAHAM: It is very interesting to hear these accounts of the use of fibrin foam, not only as we have suggested but under quite different circumstances as well. It should be remembered that it has distinct limitations and we have not recommended its use for arterial bleeding. When the arteries are easily accessible, silver clips or the endothermy will ordinarily be used. As to the availability of the material, I would only say that at present its production is in a stage of transition between the laboratory and several pharmaceutical houses. There is at present a very small supply available. It is hoped that within a few weeks larger amounts will be produced under the contract recommended by the Committee on Medical Research for appraisal both in general surgery and neurosurgery. In addition, as the armed forces contract for fibrin foam and thrombin, neurosurgeons will be asked to collaborate in controlling the effectiveness and safety of the fibrin foam and thrombin submitted by testing each preparation in the operating room. As all will agree, the services must have prior claim on what material can be produced at this time.

DR. JOSEPH P. EVANS: Is there danger that fibrin foam inserted into an opening in a large venous sinus might produce a propagating clot in the lumen of the vessel?

DR. FRANC D. INGRAHAM: In one instance, we have put a piece of fibrin foam soaked in thrombin into an opening in a dural sinus. There was no evidence of any thrombosis. Obviously, it is more desirable to keep it on the surface of the sinus when possible and it should be effective when used this way.

CAPTAIN W. B. SCOVILLE: Can the fibrin foam be used repeatedly by redipping in the thrombin solution? What is the possibility of resterilizing fibrin foam?

DR. FRANC D. INGRAHAM: I am glad that Captain Scoville has raised this question. Foam which has been in a blood-stained field should not be replaced in the thrombin solution as the thrombic activities are reduced by the presence of blood. The products should not be resterilized.

DR. ORVILLE T. BAILEY: We have had a limited experience in using fibrin foam with thrombin as a hemostatic agent in patients suffering from hemophilia. The material controls persistent hemorrhage from tooth sockets in such patients very satisfactorily but must be held in place for a period of 24 hours by means of a mechanical device.

Fibrin foam with thrombin is prepared from human proteins derived from blood plasma.

INTELLIGENCE FOLLOWING PREFRONTAL LOBOTOMY IN OBSESSIVE TENSION STATES

DR. JAMES W. WATTS and DR. WALTER FREEMAN (by invitation)

This paper was published in the July 1944 issue of the *Journal*, page 291.

DISCUSSION

DR. WALTER FREEMAN: Mr. President, Members of the Society, Dr. Watts has presented his outline in the field of psychosurgery in a selected group of individuals, individuals who are suffering from an obsessive tension state. These people have a very high intellectual activity and it probably leads to their downfall in trying to encompass too much. They go from the practical question of "what shall I do next" to the impractical and vague question of "what shall I do." The operation of prefrontal lobotomy would appear to cut down on their obsessive intellectual activity. Their ability to project themselves into the future and to envisage all possibilities is definitely impaired and, we think, to their advantage.

DR. J. G. LYERLY: My work with prefrontal lobotomy has been curtailed somewhat in the last few years because of the war emergency. In the past I have operated upon very few patients with obsessive neuroses. I think from the standpoint of study of intelligence the patients presented by Drs. Watts and Freeman are more suitable than most of those I have operated upon. In my series most cases were of involutional melancholia and the patients were so badly depressed and agitated that they would not talk or cooperate in tests before operation. It is impossible to get psychometric tests on such patients before operation. From tests after operation the psychologists conclude that, in many, intelligence is normal except for word association. For example, the patient is asked to say as large a number of associated words as he can in two minutes' time. After ten or twelve words he will stop and will not see any use in continuing. The families of some patients tell me that after operation, as far as the patient's intelligence and ability to return to work are concerned, they consider the patient as intelligent and as capable as before operation. A recent report on a patient on whom I operated two years ago is to the effect that her family considers her better than normal, and more intelligent than before; but this is just an exception. In my series of patients operated on, three-fourths have become socially adjusted and most of these returned to the same work they did before.

DR. LEO M. DAVIDOFF: I think it would be worthwhile reporting briefly on a woman with very severe post-encephalitic Parkinsonism. She was 45 years of age and a difficult problem for her family. Her Parkinsonism had been going on 17 years. During the past year and a half she developed an obsessive preoccupation with the song, "Pistol Packin' Momma." She was not able to get the words out of her head. This difficulty added to her physical distress made an impossible state of affairs. I did a bilateral prefrontal lobotomy, partly to relieve her of the distress and partly to see what effect it would have on her Parkinsonism. She was no longer disturbed by "Pistol Packin' Momma" but the Parkinsonism was unchanged.

CAPTAIN JAMES C. WHITE (U.S.N.R.): We had another patient with Parkinsonism who was obsessed by the tremor so that she couldn't face her friends. She seriously thought of suicide. The operation relieved the tremor only slightly, but after it she was relieved of her depression and promptly got a job. She no longer worries about the tremor which she still has.

DR. T. C. ERICKSON: A prefrontal lobotomy was performed in one patient with Huntington's chorea but without improvement in either the choreiform movements or the mental changes.

DR. RICHARD M. BRICKNER: I might supplement Dr. Davidoff's case with the report of a patient on whom a frontal lobotomy was performed at the suggestion of the psychiatrist. The operation tended to improve the obsessive state but had no effect on the tremor or the oculogyric crises.

DR. LEO M. DAVIDOFF: In my patient, after operation the oculogyric crises disappeared during the first week when she was in a very confused state but they gradually returned even though the compulsive thinking had disappeared.

DR. JAMES W. WATTS: We appreciate this discussion very much. There have been only two cases of Parkinsonism in our series. One was a woman who had compulsive behavior and would attack other patients and attendants without provocation or warning. Following prefrontal lobotomy she was relieved of her compulsions for about six months and then they returned. The tremor, which was quite severe, was not altered by the operation. The other patient who was disabled by Parkinsonian tremor and spasticity died from a surgical complication of lobotomy and did not live long enough to determine what effect the operation might have had.

We have been feeling our way along with prefrontal lobotomy in the treatment of pain. Many of our patients have psychalgia, but in addition to this some have had arthritis and other conditions that could have caused real pain and they have been greatly benefited. In November 1943, a lobotomy was done upon a woman with a cauda equina injury who had been suffering continuously for more than a year and who talked about her symptoms almost every moment. Following operation she no longer complained of pain but when asked specifically about it stated the pain was exactly like it had been, but she smiled when she said it. Recently a patient with carcinoma of the rectum with metastases to the liver and lungs was given the benefit of a prefrontal lobotomy. Prior to operation he was taking from one-third to one-half grain of morphine every twenty-four hours. Since operation he has not required opiates. He still has pain but mentions it only when asked about it.

ELECTRICAL SKIN RESISTANCE IN NEUROLOGICAL DIAGNOSIS

LT. COL. C. G. DE GUTIÉRREZ-MAHONEY, M.C., A.U.S.

The measurement of electrical skin resistance has been developed by Richter for the study of neurological lesions. He reported its use in the study

of lesions of the ulnar nerve after he developed the method by studying changes following sympathectomy. He also observed a variation in the skin resistance during different normal physiological states. The method has been applied to other types of neurological disease including injuries of the various peripheral nerves, spinal cord injuries, and lesions of the brain. The electrical skin resistance follows the pattern of sensory loss and is greater over the area of skin denervated. At times gradations have been found in the skin resistance comparable to areas of impaired perception of pin prick and impaired perception of light touch. Following some peripheral nerve injuries there is no change but the skin resistance can be raised following sympathetic block in a limb with a nerve injury.

DISCUSSION

DR. TRACY J. PUTNAM: I would like to ask what the weather was at the time the observations were made. We have also made observations with an instrument made by Geohegan at the New York Hospital and have not found it very satisfactory. We were not able to outline the area of anesthesia following chronic or acute peripheral nerve palsies. On thinking the matter over I assumed it was probably because the weather was very dry and cold in New York. When the weather is dry and cold the resistance of normal areas is very high. We intend to take the study up again when the hot weather is on us and attempt to duplicate the observations made below the Mason and Dixon line.

At the New York Neurological Institute we put rather more emphasis in peripheral nerve lesions and spinal cord lesions on the use of furmethide which is a powerful diaphoretic. With the use of it alone we can demonstrate areas of sweating although the results can be made more obvious with the use of starch dust. I would also like to enquire whether I understood Dr. Mahoney correctly in that lesions of the posterior roots produce alteration of skin resistance and, if so, what does he suggest the mechanism to be?

CAPTAIN JAMES C. WHITE (U.S.N.R.): I have been lucky enough to obtain one of the instruments Dr. Richter has designed for determining skin resistance and I can carry it around the wards in my brief-case. The test is a good way of watching nerve regeneration, and also of determining the extent of a sympathectomy. Dr. Curt Richter is going to speak on this subject the day after tomorrow at the American Neurological Association meeting. If you want to know, for example, whether you have removed the first or second lumbar sympathetic ganglions you have only to determine whether skin resistance is increased over the anterior aspect of the thigh. In performing this test the normal skin must be moist. It is not necessary to have warm weather, since a drink of hot tea and 10 grains of acetylsalicylic acid will usually suffice to create the same effect.

DR. T. C. ERICKSON: We have tried to pick up changes in skin resistance in the areas of partial sensory impairment resulting from protruded intervertebral discs and have not succeeded. Has Col. Mahoney tried it on such patients? On two patients with arteriosclerotic gangrene of the lower extremities we have been able to outline a clearcut line below which there was by comparison a much higher skin resistance, suggesting that it might be of value to general surgeons for the determination of the site of amputation in such cases.

DR. CARL F. LIST: Have you compared the results obtained by measuring skin resistance with those obtained with the starch-iodine test, and are there any differences? I suspect that in cases of disease of the central nervous system the discrepancies of the two methods would be considerable.

DR. BRONSON S. RAY: Stimulation of any one of the anterior roots from T-2 to T-9 will produce equal changes in the skin resistance in all parts of the hands and there is no indication of a segmental arrangement. This would probably explain Col. Mahoney's findings in his case of spinal cord injury. I am unable to account for his finding of a discrete area of increased resistance roughly in the sixth dermatome in his patient with a protruded disc between the fifth and sixth vertebrae. To my knowledge there are no sympathetic fibers coming from the sixth cervical root. I would like to ask whether any observations were made on changes in the degree of resistance in anesthetic areas on stimulation, such as stroking the foot. If such changes were shown this would indicate incomplete interruption of sympathetic fibers and would be even a better test in determining regeneration than a comparison of the degree of resistance. In the last case shown, that of the cerebral vascular accident in which normal skin resistance existed in an area of impaired sensation in the foot, were there signs of motor involvement also? We have made a few observations on stimulation of the cerebral cortex in humans at the operating table, and have found that stimulation of the motor area produces changes in skin resistance in all extremities on both sides regardless of which side is stimulated.

LT. COL. C. G. DE GUTIÉRREZ-MAHONEY: In reply to Dr. Putnam: the observations were made during warm weather and no special efforts were made to raise the temperature of the patient or to produce sweating. Lesions of the posterior roots did produce alteration of skin resistance, and the explanation may lie in the existence of efferent fibers in the posterior roots.

In reply to Dr. Erickson: I have not tested any patients with protruded intervertebral discs.

In reply to Dr. List: I have not had time to compare the starch-iodine test with the electrical skin resistance readings, but Richter did after sympathectomy and he found a striking similarity with the two methods.

In reply to Dr. Ray: In the patient with a spinal cord injury at Th-6 the electrical skin resistance in the upper extremities was not affected but there was an extraordinary elevation over both feet, which were the only parts in which the skin resistance was elevated. In the patient with the ruptured disc between C-5 and C-6 the area of increased resistance corresponded to the dermatome C-5 and a little more; it is thus difficult to explain the finding since C-5 is well above the sympathetic outflow level. The resistance was not studied while stroking a part but the current itself is a cutaneous stimulus and it was noted that the resistance fell over the exact area stimulated (4 mm.) after a few seconds, but the resistance readings were not made elsewhere within the dermatome being stimulated. In the last case there was an injury localized to the foot area of the postcentral cortex. There were no signs of motor involvement. Although there was impaired sensibility in the foot there was no alteration of the electrical skin resistance.

CHRONIC EXTRADURAL CEREBELLAR HEMATOMA

DR. FRANK TURNBULL

This paper appears in this issue of the *Journal*, page 321.

DISCUSSION

CAPTAIN W. B. SCOVILLE: Under Dr. Bagley I operated on a case of extradural cerebellar hematoma. In Hartford I had two cases of subdural cerebellar hematoma; clinical signs of particular importance were two: marked ataxia and marked hypotonicity. In the case of a unilateral clot the signs were unilateral and on the side of the clot. The extradural clot came to operation on the seventh day while the other two came on the third. Cerebellar ataxia and a high spinal fluid pressure with little or no blood in the fluid are significant signs of a cerebellar clot.

DR. JAMES W. WATTS: In 1941, I saw a boy six years of age who had fallen out of a tree a distance of approximately eight feet and landed on the back of his head. He received a laceration of the occipital region which was clipped together by his surgeon. He was not unconscious and nothing unusual happened until about 24 hours later when he became drowsy and then comatose. He moved about restlessly, and frequently both arms would go into pronation as they often do in decerebrate rigidity. There was a bilateral positive Babinski sign but no stiffness of the neck. A diagnosis of extradural hemorrhage probably from middle meningeal artery was made and while the operating room was being prepared X-rays of the skull were taken. These showed a linear fracture in the left suboccipital region just medial to the mastoid process. A right subtemporal exploration was performed and no clot was found in the extradural or subdural space. A similar procedure was carried out in the left temporal region and again no evidence of a clot was found. When the dura was opened the brain herniated through the small defect. By the time the temporal incisions had been closed the child's pulse was very rapid and his respirations were irregular. Although I had never seen an extradural clot over the cerebellum I decided to explore the left occipital region at the site of the linear fracture seen in the X-rays. Through a curved incision a stellate fracture which was slightly depressed was seen. After the bone was removed from the left suboccipital region a large extradural clot which covered both cerebellar hemispheres came into view. It was 2 cm. thick near the midline. A small opening was made in the dura and no blood was found in the subdural space. The boy remained drowsy for about 24 hours, and gradually recovered within a week without any residuals. When heard from in May 1944 he was entirely well.

DR. JOHN M. MEREDITH: In December 1939, a young colored boy, aged 9, came into our Emergency Room three times (the initial symptoms being mild) before he was finally admitted to a hospital bed two days after injury. He showed increasing drowsiness after admission, marked hypotonicity and flail-like flaccidity of the extremities and a desire to lie on one side. There was a vertical linear fracture of the posterior fossa. At operation, by our resident, Dr. J. L. Thomson, an extradural clot over the cerebellum arising from a torn torcular was removed and the patient recovered. In another case, which we had in May 1939 at the University of Virginia Hospital, the lesion was in the same location but subdural in type. That patient, a 17-year-old boy, was admitted after an automobile accident and, as in so many individuals with subdural clots, he was much sicker than would be expected with an extradural hemorrhage in the early stages. There were two linear fractures in the right temporo-occipital region. There was brain tissue resembling cerebellum, microscopically, coming from his right ear; fully an ounce of this material escaped spontaneously in a 12-hour period. His temperature rose to 102° overnight, his pulse was 110. He also, as in our first case just described, had marked generalized flaccidity and kept turning on the right side. At operation he was found to have a large subdural clot over the right cerebellar hemisphere, apparently arising from a torn superficial vein, which was coagulated. He improved markedly for a period of 7 to 8 days and regained consciousness, but he succumbed ultimately to multiple lung abscesses and empyema. Postmortem examination showed no residual clot.

It is, perhaps, a point worth emphasizing that both of our cases had a linear fracture or fractures in the posterior fossa and both of the clots were of venous origin.

CLINICAL SIGNIFICANCE OF INTRACRANIAL HYPOTENSION

DR. CARL F. LIST

Intracranial hypotension resulting from reduced intracranial blood volume or from loss of cerebrospinal fluid is, as a rule, rapidly compensated and not accompanied by serious clinical symptoms. A more severe and persistent type of intracranial hypotension is due to a combination of cerebrospinal fluid loss, diminished production of cerebrospinal fluid (aliquorrhoea), and

a reduced brain volume. This special situation is observed after evacuation of large chronic subdural hematomas (in adults) and after surgical intervention on large hydrocephalus. The clinical syndrome associated with this type of hypotension may be frankly alarming and resemble a state of increased intracranial pressure. Failure to recognize the condition and consequent faulty therapeutic procedures may be responsible for avoidable postoperative fatalities. The correct management of such cases consists of placing the patient in shock position with the head lowered, intravenous infusion of large amounts of hypotonic solutions, and inflation of the collapsed brain by intraventricular injection of Ringer's solution.

DISCUSSION

Dr. Ernest Sachs: I have seen several cases of hypotension similar to those Dr. List has described. One was a traumatic case which had been treated excessively with dehydration. The patient had been getting on very well at first but dehydration had been continued an unduly long time and when he came into the hospital he had a stiff neck and symptoms suggesting meningitis. On doing a spinal puncture the pressure was found to be about 5 mm. This was a number of years ago. Shortly before that Leriche had described a similar condition due to excessive dehydration and recommended giving intravenous water. In this patient we followed the suggestion with a good deal of hesitation, not knowing what the water would do. We started with 25 cc. Within 24 hours the patient brightened, the meningeal symptoms cleared, and the spinal fluid pressure came up to 50. Within another few days the spinal fluid pressure was normal. I have also seen cases of subdural hematoma in which the brain was markedly depressed and did not expand. In these cases I have tried all the things Dr. List has mentioned, even to injecting fluid into the ventricles, without any help in two cases because the brain had lost its capacity to expand. I would like to point out the advantages of using the artificial cerebrospinal fluid developed by Dr. Hartmann when it is desirable to replace lost cerebrospinal fluid. We use it right along in our hydrocephalus cases.

Dr. Temple Fay: Along the line of Dr. List's presentation is the problem of the dead space that remains after removal of a subdural hematoma. I have had the feeling that besides the hypotension that might exist, fluid sometimes interposes itself between the cortex and the bone flap, thus preventing expansion of the brain. We have used a drain into the subdural space, at the same time forcing fluids by mouth and vein in an attempt to swell the brain into the cavity. The drain is made with the wide end of a rubber catheter wrapped about with a rubber dam and brought out through a stab wound in the scalp. The drain allows fluid to come out onto the scalp and acts like a "flutter valve" to prevent air getting into the subdural space. When the brain has expanded into the space after 36 to 48 hours the drain is removed.

Dr. John Raaf: There is one problem bothering me. I have in mind three cerebellar cases in which tumors were successfully removed. In each case the postoperative course was uneventful until the third to fourth day when the patient became mentally confused. Recovery of all three patients finally occurred. In one instance several weeks elapsed before recovery. If hypotension was the cause I don't understand why the signs should appear after several days.

Dr. Carl F. List: I doubt that such phenomena are based on hypotension. They are more likely to be the result of secondary hemorrhages or local brain edema. Intracranial hypotension following operations for hydrocephalus and cerebral tumors occurs early and later on clears up.

In some cases it appears almost as though there were an interference in spinal fluid production. Vincent in Paris suggested that in every case of subdural hematoma the ventricle should be tapped and inflated by fluid, but that seems too radical since there is some danger in trying to tap collapsed or small ventricles. However, in some cases I have had excellent results with inflation of the ventricles. Some of the complications, such as hemiparesis and aphasia, which are attributed to collapse of the hemisphere, are perhaps due to secondary thrombosis of the superior cerebral veins which are put on serious stretch by the falling away of the cerebral hemisphere.

BLAST CONCUSSION

Lt. Comdr. William J. German (MC), U.S.N.R.

This report is based upon the study of a small group of patients several months after their exposure to atmospheric or immersion blast. The early symptomatology of "blast concussion" consisted in a variable period of alteration of consciousness, *without* retrograde amnesia. The possibility of direct trauma to the head could not be excluded. Late symptoms included headache, dizziness and "black-outs," all of which were likely to occur on postural changes. Other common symptoms were minor disturbances of memory and concentration, fatigability, irritability and apathy. Objective findings were slight or absent. The I.Q. was within normal range but scatter of intellectual performance was not infrequent. As a possible mechanism of transmission of blast pressure to the brain, a bellows effect of the chest upon vascular (venous) pressure is suggested.

DISCUSSION

Dr. John F. Fulton: It seems to me that blast injuries of the head are closely linked not only with the problem of impact concussion but also with the various sequelae of gunshot wounds of the head with high velocity fragments. Dr. Gurdjian has reported a case in which, following a gunshot wound in the cervical spine, there was contusion of the frontal lobe. This suggests that missiles of high velocity may increase for a very brief space of time the cerebrospinal fluid pressure throughout the cerebrospinal fluid spaces and produce injury at some distance from the point of impact. Commander German has mentioned the possibility of vascular transmission, especially in the instance of water-borne blast in which sudden pressure increase occurs which in turn may cause a vascular impulse to be transmitted up to the cerebrum. Dr. Geoffrey Jefferson believes strongly with other English physicians that there are no direct effects on the brain from air-borne blast. I don't know why they are so conservative on this point. Simple calculation indicates that a blast wave may travel with sufficient rapidity to give an acceleration to the head similar to that known to cause concussion from impact with a solid object. I hope someone will discuss the type of amnesia that is sometimes associated with these episodes.

Dr. R. Eustace Semmes: We have had some difficulty in ruling out the possibility that impact concussion may be the important factor in blast injuries since usually men are blown against something or fall after being blown up into the air.

Captain James C. White (U.S.N.R.): I too wonder whether the apparent cerebral blast injury sustained from this explosion wasn't simply a reaction to trauma produced by the force of gravity when the patient hit the ground.

LT. COMDR. THOMAS I. HOEN: We are seeing more and more so-called blast concussions and it has become increasingly difficult to pin the diagnosis of "blast concussion" on any one. There are always complicating factors and Commander German mentioned the question of associated infectious diseases. One case he spoke of in particular was reported to have had a subdural effusion as the result of blast concussion: we subsequently had this man under observation and although the symptoms had recurred at varying intervals since operation we were unable to verify the effusion, and just as we were about to discharge him he developed a temperature of 105° with a positive blood smear for malaria. The fact is significant that we never see real neurologic signs in blast concussion when there has been no possibility of some direct trauma to the head. Many of the symptoms ascribed to blast concussion are the result of "combat fatigue," "shell shock" or similar functional disorder.

DR. FRANK TURNBULL: It strikes me as being important that we do not allow the impression to develop that blast concussion is a frequent occurrence. I have in mind the possibility that it may take on many of the connotations of the "shell-shock" syndrome of the last war.

DR. COBB PILCHER: Experimentally the likelihood of transmission of concussion by the vascular stream seems fairly well ruled out by the work of Clark and Ward who have produced emersion blast upon animals with or without the head submerged.

DR. A. EARL WALKER: I have been impressed, as have some of the other discussors, by the probability that the syndrome in many cases may have been the result of impact of the individual's head on the ground following the blast. It will be necessary to examine the intracranial phenomena by exact techniques to determine whether a pressure wave of sufficient force to cause cerebral concussion may be transmitted to the brain.

DR. PAUL C. BUCY: The absence of retrograde amnesia with blast injuries might have another interpretation. The fact that the individual remembers hearing the explosion or seeing the blast may mean that concussion does not occur then but sometime later when there is actual contact of the head with the ground or with some object.

DR. FRANCIS C. GRANT: I am not sure the presence or absence of retrograde amnesia can be counted upon to distinguish between blast injury and ordinary concussion from impact. A prize fighter will often tell you he remembers seeing the blow start that knocked him out. As far as I have gathered, it seems to me there is not very much to separate these cases of blast injury from the ordinary concussion cases one sees in civil practice.

LT. COMDR. WILLIAM J. GERMAN: I am very glad that the discussors share my skepticism in blast injury to the brain as a distinct syndrome. I emphasized the absence of retrograde amnesia, with the same point in mind as brought out by Dr. Bucy.

I don't know if the charge in a Jap mortar shell is sufficient to blow a man off the ground. I guess it is a fairly good charge but I suspect the real injury occurs *after* he is blown from his fox hole. The term "blast concussion" is a poor one; not much better than "shell shock."

In one or two patients who sustained concussions after blast, there was definite evidence of pulmonary injury such as has been shown to occur from blast effects alone.

In regard to experimental work with emersion blast, some investigators found that with the guinea pig's head *under* water, in only four instances were there demonstrable changes in the central nervous system. The animals whose heads were not immersed either died in a very short time or, if they did not die, they remained conscious. Thus, it would seem that the direct application of immersion blast pressure to the nervous system is a very unusual occurrence.

May 18, 1944

DILATATION OF THE VERTEBRAL CANAL ASSOCIATED WITH CONGENITAL ANOMALIES OF THE SPINAL CORD

DR. A. EARL WALKER

Three cases of myelodysplasia are presented associated with a dilatation of the spinal canal at the site of the anomaly in the cervical, lower thoracic, and lumbar regions. A case of vascular anomaly angioma and aneurysm of the spinal cord accompanied by enlargement of the spinal canal is also reported. The roentgenographic and pathologic manifestations of myelodysplasia are discussed.

DISCUSSION

DR. LEO M. DAVIDOFF: I should like to ask if Dr. Walker makes use of the chart of Dyke and Elsberg for interpedicular measurements? If the enlargement of the interpedicular space over the normal is only a few millimeters the chart is useful, while a larger increase in the space limited to one or two vertebrae can be detected much more readily by charting than by simple inspection.

DR. LAWRENCE REYNOLDS: This is an exceedingly important subject, certainly for the roentgenologist. In the last case I was impressed by how little the anomaly showed if one looked hurriedly at the roentgenogram. I am certain we see a great many of these anomalies in the spine without neurological signs and symptoms. It is difficult to know how much the deformity has to do with the neurological symptoms. As roentgenologist to the Children's Hospital I see a good many roentgenograms of spines in consultation with Dr. Schreiber, and without knowing anything about the clinical signs or symptoms it is difficult to fully appreciate the possibilities of associated cord lesions in such cases. Many of these lesions appear slight and seemingly are unimportant anomalies.

DR. A. EARL WALKER: We have found the chart Dr. Davidoff mentioned to be of great value. We do feel that in children the size of the spinal canal is not quite the same as in adults. For that reason it may be difficult in children to know whether one is dealing with an abnormality or with a variation within the physiological limits of normal. In the last year or two we have seen a half-dozen cases in which there have been localized enlargements of the interpedicular spaces for which we have found no adequate cause clinically. In some of these patients who have a dilatation of the spinal canal I suspect that symptomless anomalies of the cord do exist as a cause of the widening of the canal.

THE DIFFERENTIAL DIAGNOSIS OF INTRASPINAL TUMORS AND PROTRUDED INTERVERTEBRAL DISKS AND THEIR SURGICAL TREATMENT

DR. J. GRAFTON LOVE

This paper was published in the July 1944 issue of the *Journal*, page 275.

DISCUSSION

DR. RICHARD U. LIGHT: I would like to ask Dr. Love how long and how much lipiodol affects the total protein content of the spinal fluid?

DR. R. EUSTACE SEMMES: I would like to ask Dr. Love if he has encountered any patients having both tumor of the cord and ruptured intervertebral disc?

DR. JAMES L. POPPEN: I would like to ask Dr. Love at what interspace the lumbar punctures were done routinely?

DR. J. G. LYERLY: I would like to ask Dr. Love if tumor did not cause bilateral pain more often than usually occurs with discs?

DR. J. GRAFTON LOVE: In answer to Dr. Light's question: with the assistance of the Laboratory of Clinical Pathology at the clinic, Walsh and I studied the spinal fluid protein of patients who had been subjected to injections of lipiodol, and on the first day or two after operation there was an average elevation to 50, 70 or sometimes 150 mg. per 100 cc. Usually such a reaction subsides within 76 hours. In spinal fluid examined two years after injection of lipiodol, we feel that the value for total protein is reliable and is not due to the lipiodol.

The answer to Dr. Semmes' question is yes. The first case in this series was that of an old man with paraplegia, all five of whose lumbar discs had undergone protrusion and who had a tumor in addition. Recently I removed a neurofibroma from a woman a few months after a protruded disc had been removed elsewhere. There is, of course, the question of whether she had a ruptured disc in the first place.

As to Dr. Poppen's question about the routine lumbar puncture: the puncture usually is made at the second lumbar interspace. This level is ideal for injection of air for a spinogram. It is not expected to demonstrate a block of spinal fluid in those cases in which the lesion lies in a fairly caudal position but the increase in protein content usually is about the same as it would be in fluid taken from below the level of the lesion.

With regard to Dr. Lyerly's question on bilateral sciatica: tumors do give bilateral pain more often than protruded intervertebral discs give such pain but the point is not sufficiently reliable to justify positive differential diagnosis.

OPERATIVE RESULTS IN INTERVERTEBRAL DISCS

DR. FRANCIS C. GRANT

This paper appears in this issue of the *Journal*, page 332.

DISCUSSION

DR. JAMES L. POPPEN: We have had 12 cases of spinal cord tumor in which the symptoms resembled those of ruptured intervertebral discs. One of the important diagnostic points is that patients with ruptured discs usually obtain complete relief when they lie down, whereas with neurofibromas and ependymomas, many patients have to sit up at night because of the discomfort that occurs when they lie down. If a patient has considerable pain when lying down and feels better sitting up, a spinal cord tumor should be suspected.

I agree to a certain extent with Dr. Grant. The results in cases of intervertebral discs are not always good. After following the courses of 400 cases from 18 months to 8 years, I do not feel quite as pessimistic as he does.

I believe there are several "musts" as far as spinograms are concerned. The patient with either an atypical history or findings, and the patient who has very severe sciatica of two to three weeks' duration and has had no relief from conservative measures, should enter the hospital for a spinogram. If a large defect is present, conservative measures should be discontinued. Another "must" for making a spinogram is the patient with low back pain who may have sciatica at one time or another and is to be considered for a spinal fusion. I think every patient who is to have spinal fusion should first have a spinogram to make sure no spinal cord tumor or disc is present.

Concerning the selection of cases which should have fusion combined with removal of the disc, that is a problem I think no one can settle for some time to come. But there are

certain principles we should keep in mind. A patient who does manual labor, who has protrusion of the disc with back pain and sciatica, plus an unstable lumbosacral joint, should have fusion combined with removal of the disc. It is true, however, that one cannot always tell from roentgenograms how much reaction exists around a joint or how significant an apparent anomaly may be. I believe that the patient with spondylolisthesis should always have the spine fused. Dr. Dandy and others feel that fusion is not necessary after removal of a ruptured disc and that thorough removal of the disc will give a good result. I do not know whether they will change their opinion later on or not, but I think they will.

If the patient has had only minor bouts of sciatica, physiotherapy and posture exercises can do as much as surgery and often give satisfactory results, as Dr. Grant has indicated.

Dr. R. Eustace Semmes: Dr. Grant is to be complimented on making this study. It is very important to check up on results in order to avoid undue enthusiasm. However, I am satisfied in my own mind the operation is a very worth-while procedure. We should study the patients who do not get good results and see what the trouble is. The selection of patients is important, but also important is the surgical procedure employed. About two years ago we traced 100 patients who had been operated on two years or more: 97 were working; 50 per cent at hard work, 50 per cent at light work. I couldn't tell you how many had to change their type of work. Twenty-nine, in answer to the question "Is your back weak?" said "yes." One of the most important things, as I have said, is what one does to the disc. We clean it out thoroughly and, in a good many, subsequent roentgenograms show that solid joints have resulted. I have heard of those cases of injury to the aorta Dr. Love mentioned but I still feel one ought to be able to stay inside the anterior ligament. There are now many thousands of cases operated on with a very small mortality. In 600 cases done by me in the last three years, using the procedure of curetting the disc, there have been no deaths. We had no deaths before. I think we ought not to hold back a useful procedure which I feel offers a strong probability of cure.

One more thing, I wonder in how many of Dr. Grant's patients he removed double discs? Our percentage is going up to about 33 per cent of 600 discs removed. Both lower lumbar interspaces always should be explored. Maybe it would be better to take both discs out anyway, especially in a man 45 to 50. Several of our early patients were not cured because we didn't find the other ruptured disc.

Dr. Kenneth G. McKenzie: I find great difficulty in doing the operation when I can't see well and I can't see enough by just removing the ligamentum flavum unless I put a lot of traction on the nerve root. It is amazing we don't see more recurrences than we have so far and I think the percentage of recurrences will rise considerably in any patients followed over a long period. I have always felt one important part of the operation was to remove enough bone to thoroughly decompress the nerve. It is particularly important to remove a bit of the upper rim of the sacrum for good exposure because often there is not much depth at that spot. We have been impressed with the advantages of operating with the patient lying on his involved side and the table pumped up to eye level. In particular this position allows blood to run out easily and improves the exposure. Finally, I think Dr. Grant's point of view is highly important. He is using the clinical judgment which he has developed over a period of years in dealing with tic douloureux. He has learned that it is unwise to operate for pain between bouts of pain. The patient who begs to be relieved of pain isn't going to pay so much attention to any residual pain in his back, but these people who were operated on between attacks or when they were getting better are a different problem if they have residual backache.

Dr. William V. Cone: I would like to ask how many cases with poor results have been reinvestigated with lipiodol?

Dr. Tracy J. Putnam: It was delightful to hear Dr. Grant's paper. At the Neurological

Institute also we have been rather discontented with our results and have found a large number of mistaken diagnoses and a large number of recurrences in spite of all our efforts. It seems to me that in the patient who is having agonizing pain, something has to be done. However, it is striking how seldom this occurs. Often patients are referred for operation without ever even having had their backs strapped. I think one of the first steps is to strap the back. This is almost as important a diagnostic procedure as going over the reflexes or doing a lumbar puncture.

Dr. Mount at our clinic has made a study of cases and tried to analyze them in terms of what are and what are not the indications for operation, I am glad Dr. Love raised the point about curetting the disc, which almost necessarily produces an abnormal structure. In searching about for a way to meet this problem we have thought it possible to do a fusion between the bodies of the vertebrae and have done fusions with bone screws in dogs. So far it seems feasible, but we have not done it in man. Dr. Van Wagenen has been using wedges between the vertebral bodies. This would seem a logical procedure and it would seem as if wedging the bodies apart would prevent squeezing out of more disc material. I have also felt a hesitancy about curetting, although I didn't know the ill results Dr. Love mentioned. It is interesting so many people have returned to heavy labor. We have become a little hesitant about operating in industrial cases unless the indications are clear-cut. We have also been trying to compare the advantages and disadvantages of sectioning the posterior root in these cases and I had hoped to hear the experiences of others in this regard.

Dr. Leo M. Davidoff: A year ago at the meeting I suggested a procedure which I had carried out in only a few cases—a simple fusion in the neighborhood of the protrusion, which consisted of clipping off the spinous processes and inserting them in the interlaminar space above and below the site of the protruded disc. We have been using this type of fusion on all patients. It means the patients are hospitalized a longer period—we keep them three weeks. On discharge we put on a spinal brace that is comfortable to wear. It doesn't stop patients from going back to work in a reasonable length of time. During the past year I have had occasion to operate on a few of these patients with Dr. Ober. Dr. Ober was enthusiastic and with his usual skill was able to suggest some improvements which have made it a much better procedure. The fusion requires only a few minutes in addition to removal of the disc, and although we have been doing this operation for only a little over a year I have a distinct impression that the results are better.

Dr. Wallace B. Hamby: My results of operations on discs have been published in the March issue of the *Journal of Neurosurgery* and I won't take time to discuss them. I know from experience that one's impression of what he may be accomplishing in his disc operations is often erroneous. Only statistical studies allow one to arrive at honest conclusions. One of my greatest misconceptions was that our compensation patients did badly after operation while our private patients did well. I was very surprised, therefore, to find that the statistics were strikingly parallel. Probably what this Society should do to help clarify the situation would be to appoint a committee to look into the problem on the basis of the experiences of us all and to consider the types of operation as well as the end results.

Dr. John F. Fulton: I should like to ask what the experience of those present has been with regard to the incidence of ruptured disc in various branches of the armed services. I have happened to come across cases in the Air Forces personnel, particularly those assigned to the carriers. The flat-top, you know, has a small space to land on. The ship usually hits and stops with a double jerk. Whether or not that contributes to the rather high incidence of ruptured discs in the group I don't know. Air Vice Marshal Symonds was at first of the opinion that service personnel could seldom be returned to active duty after a disc operation. He continued of the same opinion until about nine months ago, since when, following a change in surgical handling of such cases, many Air Force personnel have returned to active duty. I would sec-

ond the proposal just made by Dr. Hamby. It would be a real service to our armed forces if some unanimity of recommendations could be arrived at.

CAPTAIN JAMES C. WHITE (U.S.N.R.): In the Naval Hospital in Chelsea ruptured discs form about the second greatest group of patients I see. Head injuries constitute the largest number, while ruptured discs are slightly more frequent than peripheral nerve injuries. After these men have been incapacitated for three or four months they are admitted on the Orthopedic Service. As the time in which service personnel can be treated conservatively is limited, the orthopedic surgeons soon get after me to see if the patients shouldn't have the discs removed. I have been using pantopaque spinograms followed by operation if there is a well-defined deformity. In the fall we should have fifty cases with a six-month to three-year follow-up. My impression is that the results are going to be pretty good. In that group of fifty cases there were two cauda equina tumors. One we picked up in the routine spinogram, while the other had undergone an unsuccessful operation for disc elsewhere.

MAJOR BARNES WOODHALL: I regret that my predecessor at the Walter Reed Hospital, Lt. Col. Spurling, is not present at this meeting. We all know that he is a surgeon deeply interested in this problem. At the present moment, peripheral nerve injuries represent our greatest responsibility in the Zone of the Interior; discs remain the second. We are dealing for the most part with young, vigorous soldiers and when the feasibility of operating upon these lesions was discussed originally, I believe that we promised that we would return at least 30 per cent to duty. I have had a somewhat unique opportunity of comparing my experience with disc surgery in civilian practice to that in military service. I had completed in detail a study of the results in some 300 civilian cases beginning in 1937 but at present these results are tucked away in the Duke Hospital attic. However, as I recall them, about 83 per cent did fairly well. The results in the Army so far seem somewhat similar. It is our impression that we achieve somewhat better results among officer personnel, in one hospital as high as 95 per cent returned to duty. On the other hand, a considerably lower percentage of enlisted personnel returned to duty and their type of duty was usually altered to a less strenuous one. We in the Army would be very happy to cooperate in a study of end results. In fact, one has already been ordered by Brigadier General Rankin. We should be interested in having some part in this study proposed by the Society especially in relation to the proposed standards for recovery. So far we have not noticed any particular type of injury as the precipitating factor in this disability. It appears in most cases to result from the strenuous wear and tear of Army life. The operative technique that we follow is one marked by a minimal unilateral exposure, removal of ligamentum flavum, minimal bone resection, if any, and controlled curettage of the interspace.

MAJOR FRANK H. MAYFIELD: My experience in the treatment of intervertebral discs has been essentially the same as that described by Major Woodhall—officers do well, enlisted men less so. I believe, however, that this may reflect the ability of officers to adjust their activities better than the enlisted men rather than any difference in the moral integrity of the two groups. The trials of field training in the American Army are tough. Most men will agree that the training is more severe than anything they have encountered in combat. I believe that a man who has had a disc removed has a less durable back than one who has had no disc injury, and that symptoms will return, even though mild, if a patient is permitted to go on to complete exhaustion. Healthy muscles splint the back, and I am sure that fatigue such as is attendant to hikes of 15 to 20 miles will produce symptoms in many instances. It is my feeling that if these extremes of physical exertion are avoided approximately 80 per cent of the enlisted men operated upon will return to and remain on duty. This is, of course, an estimate.

DR. LAWRENCE REYNOLDS: I don't know whether it is in order for a roentgenologist to enter the discussion when there is such a difference of opinion over what should be done with

a ruptured disc. I think Dr. Grant gave the most significant paper I have ever yet heard on the subject. He raised a very pertinent question, namely, where were these discs before 1937? I don't know personally that I have ever known of a patient who played football developing a ruptured disc. I am reminded very much of the question a farmer asked of a famous physician: "Doctor, you are a great doctor, what causes pain in a woman's back?" And the doctor replied, "Damned if I know." I think this is true of so many of these cases. The orthopedists can cite various causes for sciatica and pain in the back. I think five years from now we won't hear so much discussion about discs at this Society, as the diagnosis and the therapeutic measures instituted will have assumed their proper place in the treatment of low back pain.

Dr. Albert S. Crawford: It is a good thing that Dr. Grant has opened up a fuller discussion on this problem. I wonder if Dr. Reynolds might be correct in his prediction? I would agree with him to the extent that five years from now we may be more moderate in our enthusiasm over the results so far achieved. We neurological surgeons, representing one of the youngest surgical specialities, have welcomed new additions to our field of endeavor. This has proven to be a dramatic addition, and it will probably remain a really effective one. But I have a feeling that for it to remain permanently so, more accurate and definite criteria for operating and for judging results must be developed. I have made a study of over 100 of our cases and the end results are about the same as those of Grant and Hamby. The type of operation varies from complete uncapping of nerves to peek-hole removal of ruptured discs. I believe Hamby's suggestion of a combined study is a good one. Let a committee outline the problem and let us all use a commonly accepted plan of study and of reporting results.

Dr. John M. Meredith: I should like to ask Dr. Love in what percentage of his patients he is now doing spinal fusion after removing discs? We have made a practice of employing fusion in verified disc cases with marked spondylolisthesis or, at the suggestion of the orthopedist, in cases with lumbar scoliosis or a definitely unstable lumbo-sacral joint in which a disc has just been removed. This, however, actually amounts to the occasional case only. We have operated on patients with all of the symptoms and signs of a ruptured disc only to find no such lesion present. In such cases we have sometimes, as Dr. Putnam mentioned, divided extradurally about half the sensory root affected with the idea that perhaps the root was actually being compressed peripherally at the foramen. It is our impression that such patients have obtained the most relief in cases of negative exploration for a disc. We also have had the experience of obtaining normal spinograms with lipiodol only to find in some cases that exploratory operation, because of pronounced clinical symptoms and signs, disclosed a ruptured disc of at least moderate size. It is this kind of experience that lends support to the opinion of those who contend that preoperative spinograms, with lipiodol or air, for diagnostic purposes are unreliable.

Dr. J. Grafton Love: I am pleased with the amount of discussion that has arisen. I would be the last to insist that everybody who is subjected to this operation is cured by it. I know of no surgical or medical procedure that will cure every patient to whom it is applied, but I do not know any procedure that gives the same satisfactory results that this operation affords. After all, removal of a tumor of the spinal cord does not always restore the patient to a completely normal condition—why should invariably good results be expected when operations are performed for protruded discs? Patients older than forty years, with hypertrophic changes in the spinal column, are likely to have some backache, whatever else may be present. I have operated for ruptured disc on one physician who also had Paget's disease. The sciatic pain was relieved but the pain attributable to Paget's disease continued. Many factors must enter into consideration of end results. When I began this work I was a young surgeon in the Mayo Clinic, with many older men to advise me. Consequently, I had to be very careful and very convincing. I was not expected to operate for protruded disc until the patient had been examined by an orthopedic surgeon. Moreover, after the operation, the orthopedic surgeon

re-examined the patient. It was only after our orthopedic colleagues had been convinced that we neurologic surgeons could cure the patients that we felt free to carry on with the disc operation. We feel that our results fully justify the procedure although they are not 100 per cent successful and we are anxious to have any suggestions that might improve the operation.

I agree that the patient should have conservative treatment first and frequently we make the diagnosis without doing lumbar puncture or operating. Many times patients who might profit by more prolonged nonoperative treatment more or less force us into operating on them. A review of a series of patients treated at the Mayo Clinic without operation showed very satisfactory results from conservative treatment. Unfortunately, many of the patients who formed the basis of that review subsequently had trouble and underwent operation. When I first became interested in the subject of sciatica, epidural injections were employed by many physicians and I was taught that it was a good procedure, yet my personal experience with it soon taught me it was far from satisfactory.

With regard to Dr. Meredith's question concerning fusion: this is not yet settled and concerning it the orthopedic surgeons will have the final say. Recently I did have time to look up the number of my own cases in which fusion was performed in the last year. In about 20 per cent of my cases fusion was performed but, frankly, I do not believe we need to effect fusion in so many cases. Whether or not fusion shall be performed depends on the type of case. Some years a surgeon might encounter a relatively large number of cases of spondylolisthesis and this condition is a definite indication for fusion. Patients with "prespondylolisthesis" also progress better if fusion is effected. In both types of cases just mentioned, fusion should be done even if a tumor of the spinal cord is removed. The patients with simple narrowing of an interspace or with minimal hypertrophic changes do not require fusion.

Dr. Reynolds said he never had heard of a football player with a protruded disc. I have operated on several. But ordinarily golf and bowling are particularly hard on patients with bad backs.

This matter of herniated discs being comparable to a wet baby's head or a dry baby's head brings up the point that often fluid does drip from fragments. I think that is one of the reasons patients get relief from conservative treatment; the edema subsides and thus the mass which compresses the nerve roots subsides. Of 100 specimens studied at the clinic, 22 were very edematous. The nucleus pulposus can absorb fifteen times its volume of fluid.

Dr. Francis C. Grant: I am glad that Dr. Love discussed this paper because he has answered most of the questions.

We collected the data that we have outlined to you because I did not believe that in our hands the results of surgical removal of ruptured intervertebral disc seemed as favorable as the reports from other clinics. A great deal has been written about the diagnosis and technique but not much about follow-up. I am afraid I must disagree entirely with Dr. Love's statement that the results are extremely favorable. Our general impression was that the operative results were not as happy as we had hoped, and the actual information contained in the paper here given I am afraid goes far to confirm this opinion.

Dr. Cone asked what we thought was the cause of the poor results in those cases in which they had occurred. We have not exact information on that point. My impression is that the poor results are due to the fact that the main cause of the patient's back pain was not the disc which was removed surgically. I cannot, however, confirm this statement.

We have had no experience with fusion. Unfortunately, we cannot get an opinion from our Orthopedic Department as to the propriety or impropriety of immobilization of the back.

Our chief purpose in collecting these figures was to stimulate others to do so, so that we could have some valid information as to the end results of the removal of discs in a large group of cases. We may then be able better to decide in which individuals operation can be performed with every chance of success, and refuse operation to those persons in whom, in spite of a medical syndrome suggesting disc, experience shows that operation will not be beneficial.

PLASMA CLOT SUTURE OF NERVES

Dr. I. M. Tarlov

Stimulated by the work of Young and Medawar, a technique has been developed using autologous plasma for suturing peripheral nerves. In those instances in which strain exists at the suture site, tantalum wire tension sutures are used in addition to the plasma clot. By the plasma clot technique it is possible to obviate many of the disadvantages of the conventional silk method and to obtain better apposition at the suture site. The method has been applied to human cases with encouraging results. The technique is described in a series of lantern slides and by a motion picture film.

PERIPHERAL NERVE INJURIES

Lt. Comdr. Thomas I. Hoen (MC), U.S.N.R.

Presentations of cases selected from a series of 40 examples of peripheral nerve injuries.

Case 1. Brachial plexus paralysis; neurolysis; recovery. [Motion pictures.] This is an example of extensive paralysis from extra-neural scar, secondary to blood-vessel injury. Early evacuation of hematoma is recommended in such cases.

Case 2. Median nerve paralysis. Laceration of wrist 4 years previously. Plasma clot suture. Tinel sign 14 days; recovery of sensation 28 days; muscle atrophy and late (3 months) return of motor function, preceded by drop in chronaxie. [Motion pictures.]

Case 3. Laceration of posterior cord of plexus with complete circumflex and partial radial palsy (brachioradialis and extensor carpiradialis). Plasma clot repair. Marked improvement in function of shoulder (substitution). No nerve recovery as yet. [Motion pictures.]

Case 4. Ulnar nerve paralysis. Plasma clot repair after 5 months. Drop in chronaxie did not precede return of muscle activity. Complete recovery 4 months.

Case 5. Combined median-ulnar palsy from laceration above wrist. Plasma clot repair of ulnar; neurolysis of median. No return in either nerve in 5 months. (? other factor than nerve continuity.) [Motion pictures.]

Case 6. Median nerve repair (plasma clot) at wrist. Recovery of sensation, nerve function and chronaxie in 19 days.

The method of assessment of results is described. Photographic records in motion pictures of paralysis and sensory loss, periodic electrical studies of nerve-muscle mechanism, and histologic studies of nerve ends are presented with a discussion of the correlation between these factors and the time interval between injury and repair.

The difficulty of clinical evaluation is pointed out and clinical improvement through functional substitution emphasized.

DISCUSSION

DR. PAUL WEISS: I consider it a great privilege to be allowed to address you. Progress in matters of nerve repair will come from the cumulative effects of many small improvements rather than from any one dramatic discovery. It will have to be guided by insight into the requirements of nerve growth. While earlier work has comprehensively described the microscopic picture of nerve regeneration, analytical understanding of the physical and chemical realities involved is of relatively recent date. Indications are that the growth potential of a nerve fiber is limited; a fiber advancing at 3 to 4 mm. per day is apparently giving its maximum output. No artificial measure is likely to succeed in boosting this rate. All we can do is to provide conditions under which the nerve fiber can realize its maximum growth capacity. We can facilitate the transit from proximal to distal stump, and eliminate potential obstructions, such as the scar. The scar not only deflects and arrests many nerve fibers, but its constriction prevents the regenerated ones from gaining in width.

The desirata of optimal nerve regeneration are: (1) straight, unimpeded oriented outgrowth; (2) lack of branching and commingling; (3) ample serous spaces for the later expansion in width of the regenerated fibers; (4) exclusion of fibrosis. Suture methods must be rated by their conformance with these requirements.

Plasma suture may meet some of them. Its avoidance of stitching is a decided advantage. It also aims to insulate the junction from extraneous tissue. However, the enclosed epineurium still provides material for potential scars. The scar problem, as I see it, is not so much one of the presence of fibroblastic tissue as of its orientation, and this orientation depends on the pattern of tensional stresses. Epineurial growth along the surface of a nerve junction remains innocuous. But if blood plasma seeps between the nerve ends, its subsequent contraction with adhesions to the sheath might produce inroads for epineurial tissue and establish a center of fibrosis and fiber confusion. Pictures of plasma suture published by Gutmann and Sanders from Young's laboratory (slide) confirm this. However, the slide Dr. Tarlov has just shown illustrates a remarkable improvement over their results.

The hazards of internal scar formation are reduced in the technique of sutureless sleeve splicing of severed nerve ends, as developed in our laboratory. By a combination of factors, this method satisfies all four of the above requirements and leads to as nearly perfect reweaving between severed nerve stumps, or nerve stumps and grafts, as can be expected (slides). With the use of an artery cuff or a self-sealing, elastic tantalum sleeve including a short blood clot between the nerve ends, almost no evidence of a "suture line" can be seen after a few months in animal experiments (cat, monkey). Replacing whole blood by a clot of plasma inside the sleeve produced much messier regeneration and considerable fibrosis; blood plasma between the nerve ends is too compact for optimal nerve growth.

It is too early to pass final judgment on either method. Moreover, there will be cases in which only one or the other or neither would be applicable.

Aside from this general comment, I wish to raise the following specific questions. If a stitch of wire is used in plasma suture to hold the stumps, why the concern about the tensile strength of the plasma? It has sometimes been stated that plasma coats are superior to solid sleeves because they do not interfere with vascularization. Since ample vascular supply is provided from the nerve ends, why the need for extraneous vascularization? On the other hand, if the plasma coat is pervious to blood vessels, why not likewise to extraneous scar tissue? If blood plasma fuses with the surface of the nerve, there forming a new sheath, what prevents it from seeping in between the nerve ends to form a potentially fiber-forming partition? These points are raised more for clarification than as objections.

As for the basic policy of the reported research, namely, the use of objective standard criteria for the assessing of the functional results of nerve regeneration, one can have only the highest praise. Such critical assessment will eliminate much of the misjudgment and many of the misinterpretations of the past.

DR. JOHN F. FULTON: I would like to hear Dr. Weiss discuss the pros and cons of the various types of sleeve: tantalum, fibrin film, arteries and veins.

DR. PAUL WEISS: To be useful, a sleeve must form no adhesions with the interior of the nerve. Blood plasma coats may merge with the inside of the nerve. Veins remain distinct but are too flabby. Arteries are quite satisfactory but those of proper specifications are hard to procure. Frozen-dried arteries have proved adequate, but do give some internal adhesions. Thus far, the tantalum sleeve has proved best in the experimental tests, but there are other materials coming up which may prove even superior. Many materials have been tried in the past for wrapping or tubulating nerve stumps, but those methods, whose results have mostly remained far short of their objectives, resemble sutureless sleeve splicing only superficially.

LT. COMDR. WILLIAM K. LIVINGSTON: I am not qualified to evaluate the various methods of nerve suture. I haven't used plasma suture at all, and have used the tantalum sleeve in only twelve cases. In four of these I removed the tantalum about a month after the sleeve had been applied. I found a smooth, glistening membrane forming on each surface of the tantalum and separated from it by a small quantity of watery fluid. The metallic sleeve can be readily removed, leaving the nerve thinly coated with what appears to be a coagulum rather than firm scar tissue. My patients have been operated on too recently for me to state how successful the regeneration of the nerve will be, but the method has promise.

I think the use of tantalum sleeves must be carefully evaluated. I had only one patient that developed infection. This marine had a large piece of bullet jacket in his wrist and the wound had drained for some weeks following his injury. I removed the foreign body and did an end-to-end anastomosis of the divided ulnar nerve. To protect the suture line from the dense scar I applied a tantalum sleeve. The scar subsequently broke down at one spot, but healed up again in spite of the persistent presence of the sleeve.

I saw Dr. Weiss' experiments with tantalum and with nerve grafts. I was very much impressed by the lack of tissue reaction occasioned by the tantalum and the evidence of regeneration across the line of anastomosis shown in his microscopic slides. His results with nerve grafts protected by tantalum or arterial sleeves are remarkable. I examined one cat in which a long graft had been inserted in the sciatic nerve about a year previously. I could not tell from the cat's actions which side had been grafted. I would not have believed that such results as he has reported were possible unless I had myself identified the graft under the dissecting microscope.

I enjoyed these papers dealing with peripheral nerve problems and was particularly interested in the clinical aspects of Commander Hoen's presentation. His first case was perhaps the most dramatic, but we must be cautious in attributing the recovery that may follow operation to the neurolysis. I have explored a number of cases of brachial plexus injury in which there is no anatomical discontinuity of the nerves, yet strong stimulation with the Hinsey-Geohegan stimulator fails to indicate any transmission of the impulse. In most of the cases of this type recovery is good whether or not one does a neurolysis. If there is evidence of a change in the sensory and motor disturbance within a few days of operation, we are justified in attributing this change to the neurolysis. If the change takes place weeks after the operation, then one must be very conservative in evaluating the part played by the neurolysis, because I am sure that injury to nerves from the close passage of high velocity projectiles can cause a complete loss of function for weeks or months, and then the nerve may quite suddenly show signs of spontaneous recovery.

DR. I. M. TARLOV: The question Dr. Weiss raises about the importance of the tensile strength of plasma is a natural one. One has to consider not only the longitudinal strain, well taken care of by the use of tantalum wire tension sutures, but also shearing forces acting on the site of the suture and the result of pressure from neighboring muscle or lateral acting forces transmitted from other tissues. Upon nerves sutured with plasma clot we have made measurements of forces, including shear, similar to those exerted upon sutured nerves in the body by lateral pressure from adjacent structures. The values obtained from these experiments were roughly of the same order as those for the breakage strength of nerves sutured with plasma

clot. The use of plasma clot in addition to tantalum wire tension sutures is therefore indicated for nerve suture since the latter alone will not prevent shearing forces from displacing the nerve ends. Plasma clot is further advantageous in that it forms an epineurium which prevents the ingrowth of connective tissue at the suture line.

I did not intend to refer to the use of tantalum cuffs to surround the suture site. However we have done some experiments which bear on this point and it seems to me that tantalum cuffs are unnecessary when one uses plasma clot since the latter, by virtue of its conversion to an epineurial sheath, prevents the intrusion of fibroblastic tissue at the suture line.

The objection to the use of tantalum foil on the ground that it prevents blood vessels from entering the sutured nerve from the surrounding tissue is probably not a valid one since the longitudinal blood supply of the nerve seems to be adequate. However, in cases of nerve grafts the use of tantalum foil to surround any considerable proportion of the graft is a matter of great importance. It is possible to demonstrate that one of the main factors in determining the "take" of a nerve graft is the adequacy of its blood supply. Grafts depend for their vascularization on the ingrowth of blood vessels from two sources, first, from the host stumps and second, from the surrounding tissue. The use of tantalum foil or any impermeable membrane to surround the nerve graft, or any considerable portion of it, is unwise since blood vessels are thus prevented from entering the graft and necrosis, either partial or complete, may result. In the experimental animal we have actually seen necrosis of the graft result from the use of tantalum foil around it.

The pictures that Dr. Weiss showed of Young and Medawar's very admirable work must be viewed in their proper time perspective. They were early attempts and like many early attempts they sometimes seem rather crude in the light of subsequent developments. It is not important that they did not get altogether satisfactory orientation of fibers at the suture site —they employed heterologous substances for nerve suture without the use of the mold. The important point is that these investigators conceived a new and promising technique in an attempt to better our method of suturing nerves, a method which has since been improved.

It is rather comforting to hear Dr. Weiss state that he has no objection to blood at the suture site if it is not excessive, but it is rather upsetting, so far as my notions are concerned, since I have felt on the basis of histological studies that blood at the suture site resulted in fibrosis and interference with the proper downgrowth of nerve fibers. We have gone so far as to devise a special nerve hemostat with its jaws covered with airfoam rubber in order to arrest bleeding from the nerve stumps completely before suture is undertaken.

So far as passing final judgment on the technique of plasma clot suture is concerned, this cannot be done at present. More experience will have to be gained with the use of this method. One can, however, state that very good apposition of nerve ends can be obtained with plasma clot suture and that the results thus far appear to be encouraging and warrant further clinical use of the technique.

Lt. Comdr. Thomas I. Hoen: I don't believe there is any comment necessary except to thank Dr. Livingston for his remarks. In brachial plexus injuries the only point is perhaps that it is wiser to evacuate the clot early and not wait 5 to 6 months when there would be a dense cicatricial mass. We believe that when first-line facilities are adequate, the patients with brachial plexus injuries, with massive swelling and ecchymosis, should have the clot evacuated by simple incision and washing out of the clot.

Dr. John F. Fulton: I believe the Harvey Cushing Society would render a national service if it could promptly issue some type of brief monograph on the peripheral nerve problem. I make the proposal because revision of the N.R.C, military manuals is not imminent. That being the case, we have a unique opportunity now to correlate the material collected so rapidly in the last year or two. If the Society could sponsor such an undertaking I would like to think that some one of you, perhaps Captain White, would act as the chief editor and appoint authors, and see if in the next six months we could get out an authoritative statement on the problem.

THE MINIMAL ANATOMIC AND PHYSIOLOGIC BASIS FOR LUMBAR SYMPATHECTOMY IN VASOSPASTIC ANEMIAS OF THE LOWER EXTREMITIES

Dr. Rupert B. Raney

The segmental distribution of the sympathetic nerve supply to the vascular system is discussed in relation to the necessary surgical resection for sympathectomy affecting the lower extremities.

Technical details of the operation are illustrated with lantern slides and a 16 mm. kodachrome motion picture.

DISCUSSION

Captain James C. White (U.S.N.R.): Dr. Raney has shown us a beautiful piece of motion picture photography and a nice anatomical approach. However, I have seen one or two recurrences when only a single lumbar ganglion was removed, and believe that a greater length of sympathetic trunk must be removed to prevent occasional regeneration. The approach Smithwick and I have advocated in our book is by a muscle-splitting extraperitoneal incision. The patient is upset extraordinarily little by such an operation and may get up after spending only a day or two in bed. Most patients are able to do light details on the ward by the end of a week. Of course, the retroperitoneal approach requires two operations, but these can be done within a week of each other, Actually, I believe, two extraperitoneal operations are safer than a single one by the transperitoneal route; the patient is likely to have far less postoperative discomfort, and he can return to active military service in a shorter time.

Dr. J. Grafton Love: I would like to ask whether or not the operation is followed by sterility in the male.

Dr. Bronson S. Ray: For the sake of the record I would like to draw attention to an error in the anatomical diagram Dr. Raney used. This shows the uppermost segmental level, giving rise to sympathetic fibers to the lower limb, to be T-12. We have found the segmental level extends at least as high as T-11 and occasionally to T-10.

Dr. Carl F. List: Has Dr. Raney seen any evidence of regeneration after taking out only one sympathetic ganglion?

Dr. Donal Sheehan: I would like to raise the question whether the operation is anatomically sound. In the first place, it is not possible to speak with any certainty of a "fourth" lumbar ganglion. The duplication and fusion of the embryonic sympathetic anlage result in a highly variable pattern in the adult. There may be only three or as many as seven or eight recognizable ganglia in the lumbar region. Furthermore, in the lumbar region in man, the rami are of two kinds, oblique and transverse. The "oblique" are for the most part white rami and there are one, two or sometimes three such rami emerging from the first and second lumbar spinal nerves. Those from the second lumbar may enter the sympathetic chain anywhere along its course between the levels of the second and fourth lumbar vertebrae. The ganglia in this particular region provide some of the post-ganglionic fibers to the lower limb. They would not be necessarily interrupted by the removal of the "fourth" lumbar ganglion alone. The proof of the efficacy of the operation must, of course, be sought in the clinical results, but there is certainly doubt in my mind whether this operation, as advocated, would provide an adequate sympathectomy of the lower limb.

Dr. James L. Poppen: Dr. Raney should be commended on the excellent technique as demonstrated by his movie. Dr. Raney apparently is an excellent general surgeon, but I do not believe that neurosurgeons, not familiar with abdominal conditions, would want to try his procedure. After all women also require sympathectomy and they may have adhesions

in the pelvis, which would add to the difficulties of the operation, whereas the approach from the lumbar area presents no difficulty whatsoever. We used to perform sympathectomy through the abdomen and often felt called on to explore the abdominal contents as well. If a pathologic condition were found, there was always the temptation to do something besides the sympathectomy. This temptation is obviated by the lumbar extraperitoneal approach. Furthermore, my main objection is that the abdominal operation described may increase the possibility of postoperative thrombosis and embolus formation. I believe, also, that more radical removal of the lumbar ganglia is necessary.

Dr. Rupert B. Raney: The transabdominal approach, when bilateral sympathectomy is indicated, has been employed since both sides can be done through one incision. I have, perhaps, been influenced to use this approach because of general surgical training prior to entering the special field of neurological surgery. For a unilateral sympathectomy, however, I have routinely used the retroperitoneal approach.

With regard to proof of adequate sympathectomy on section of the fourth lumbar ganglion starch-iodine tests were made postoperatively, which showed an absence of the sweating phenomenon to a level slightly below the knee. Possibly the mild climatic conditions in Southern California may have influenced the results, and I do not know how the sympathectomy described would stand up in colder climates. Under these conditions, clinical relief was obtained. I have no data on whether or not a sterility occurred. Potency did not appear to be altered.

With regard to Doctor Ray's question, the illustration shown was not based on anatomic dissection of the sympathetic chain; it was modified from the map of dermatomes prepared by Henry Head and used for illustrative purposes.

EOSINOPHILIC GRANULOMA OF THE SKULL
REPORT OF A CASE

MAJOR JAMES B. CAMPBELL, M.C., A.U.S. AND
CAPTAIN EBEN ALEXANDER, JR., M.C., A.U.S.

(Received for publication July 25, 1944)

In 1940, two papers appeared in the American literature, one by Otani and Ehrlich[6] and the other by Lichtenstein and Jaffe,[5] dealing with a benign granulomatous lesion of bone which has been called solitary granuloma or eosinophilic granuloma of bone. Previous to that time there were occasional references to the German literature concerning rare cases of the same condition, but no correlation was made of the widely scattered reports. Other case reports have appeared since then by Bass (1941),[1] and by Kernwein and Queen (1943),[4] and the latter stated that only nineteen cases of eosinophilic granuloma had appeared in the literature up to that time. They, however, did not include the excellent study by Green and Farber,[2] published in 1942, in which a forthright attempt was made to correlate this condition with others, somewhat more widely publicized in the literature, namely, Hand-Schueller-Christian disease and Letterer-Siwe disease. Previous to that Otani and Ehrlich[6] had noticed the similarity of microscopic sections of their cases of eosinophilic granuloma to those of Hand-Schueller-Christian disease, but no correlation between the two conditions was drawn and it was felt by them that the etiology of solitary or eosinophilic granuloma of bone was probably local trauma.

The etiology of eosinophilic granuloma of bone is still not definitely known but there are certain points about the reported cases which make a diagnosis possible. It is a granulomatous lesion of bone which affects children or young adults predominantly and shows a distinct tendency to affect males more often than females. The lesion is not always solitary as was first considered, since in several instances multiple bones have been affected, but in approximately half of the reported cases the skull has been involved either alone or in combination with other bones.[1] No cases are recorded in which any bones of the skull other than those of the cranial vault were affected, and apparently the lesion has not been noted to affect the bones of the hands or feet. The condition is rarely associated with any significant degree of generalized illness, and the initial complaint as a rule has been local pain. When the lesion has affected a bone that is superficially located under the skin, local heat and tenderness have been prominent. Occasionally lesions situated in strategic locations, such as the vertebrae, have given symptoms referable to a system or organ. Some cases have been free of complaints, having been discovered incidentally when x-rays were taken for some other reason.

By x-ray the lesions are usually radiolucent areas which may vary widely in size. In the skull they tend to be circular, sharply outlined, often giving a punched-out appearance. There is nothing really distinctive about the

Roentgenographic appearance and solitary lesions may closely resemble bone cysts, osteomyelitis, or even primary or metastatic malignancy.[2] Multiple lesions often suggest multiple myeloma and some cases are exactly similar to Hand-Schueller-Christian disease. The areas seen by x-ray frequently develop quite rapidly, and, as will be later noted, often resolve just as rapidly after treatment.[3]

In many of the cases of eosinophilic granuloma of bone, a very mild eosinophilia varying between four and ten per cent has been found,[5] particularly in the early cases. There has been no other consistently abnormal laboratory finding although studies of blood lipids, blood cholesterol, total protein of the blood, serologic tests for syphilis, and urine tests for Bence-Jones protein have been repeatedly carried out.[4] Many lesions of eosinophilic granuloma have been biopsied or removed, and cultures or special studies for the presence of a virus have been made in numerous instances. So far all of these studies have met with negative results.

PATHOLOGY

Eosinophilic granuloma usually starts as a well localized lesion in the medullary cavity, tending to erode, expand, and perforate the cortex. In the calvarium, it may erode either inward or outward and several cases have been recorded in which a considerable area of the dura underlying the bone lesion has been directly involved. There have not been cases in which the brain has been involved, nor does the tumor apparently have any tendency to erode into blood vessels. Grossly the tumor appears soft, sometimes quite hemorrhagic and gives the distinct impression of being malignant.

Microscopically the picture varies considerably from case to case, apparently depending on the length of time that the lesion has been present. As a general rule, the lesion is characterized by the presence of compact aggregates of large phagocytic cells, called histiocytes by some, with conspicuous collections of eosinophiles.[3] Indeed the eosinophiles may be such a prominent feature of the picture as to stain the entire field red to first inspection in a hematoxylin and eosin stained slide.

The publications of Green and Farber[2] and of Lichtenstein and Jaffe[3,5] have dealt most comprehensively with the correlation of this disease process and its possible etiology. For a detailed discussion of this subject one should refer to those papers. In spite of the fact that Otani and Ehrlich[6] noted similarities of this condition to Hand-Schueller-Christian disease, they felt that, since a history of trauma preceding the development of eosinophilic granuloma was so common, it was probably an etiologic factor. However, since that time, Farber[2] has carefully studied several cases of eosinophilic granuloma of bone, and he is of the opinion that this disease is actually the mildest and most benign expression of a generalized disease process of which Hand-Schueller-Christian disease is the most insidious and chronic form (occurring in older persons generally) and Letterer-Siwe disease is the most malignant and severe (usually occurring in infants or young children). This concept has received added impetus from Jaffe and Lichenstein[3] who state that in certain

stages the lesions of both Hand-Schueller-Christian and Letterer-Siwe disease are indistinguishable from those of a typical early lesion of eosinophilic granuloma. They therefore feel that the three conditions, which show very little similarity clinically except from the Roentgenographic point of view, are, from the pathological point of view, related expressions of the same disorder. The lesions of all three, they feel, are characterized at their start by the presence in them of large numbers of histiocytes. They hypothesize, with considerable justification, that the basic disorder is an inflammatory histiocytosis developing in response to an unknown infectious agent.

TREATMENT

Whatever be the cause of eosinophilic granuloma, it is apparent to all students of the subject that the prognosis is universally good. Since it is not possible to make a final diagnosis of the condition clinically or by x-ray, it is necessary to at least biopsy the lesions that are found. Many such lesions after simple curettage and biopsy have gone on to complete healing and disappearance without evidence of recurrence for a matter of years, or as long as the cases have been followed.[2] Surgical extirpation of tumors, particularly those of the skull that involve the underlying dura, has also been satisfactory and has not been followed by recurrence. Postoperative x-ray therapy has been given frequently but does not seem to be necessary. Green and Farber[2] have treated some lesions by x-ray alone, using 1500 R. Units through two fields over a six-day period, with satisfactory disappearance of the lesions. These were cases in which tumors of other parts of the body had been previously biopsied for pathological study. Jaffe and Lichtenstein[3] have observed the healing of eosinophilic granulomata that have received no treatment, and have examined microscopically sections of tissue removed from the site of a lesion previously clearly demonstrated by x-ray. In these cases they felt that the healing had occurred by resolution rather than by scarification and fibrosis. The exact method of healing has not been studied in a sufficient number of cases to warrant a final statement.

CASE REPORT

Although eosinophilic granuloma is a relatively rare disease, a fairly large percentage of the cases, at least half, both those of single and of multiple lesions, occur in the skull. The following case report of an eosinophilic granuloma which occurred in the left frontal bone of a soldier in the South Pacific Theater is presented. The tumor was removed and identified in an overseas numbered General Hospital, and the patient was later evacuated to the United States where further investigation was carried out and the skull defect, left by extirpation of the tumor, covered with a tantalum plate.

A male, aged 27, was admitted to a numbered General Hospital in the South Pacific Theater 18 April 1943 with the chief complaint of painful swelling of the left frontal region.

Past History. He had had occasional headaches of mild character, relieved by aspirin for years. He had also had occasional ringing in the ears, particularly the left, for some months prior to the onset of the present illness.

Family History. The patient's father had suffered from headaches and ringing in his ears for many years. The cause of his complaints was not known. The brother of the patient had had progressive loss of hearing bilaterally; cause unknown.

Present Illness. In January or February 1943 the patient accidentally bumped the left side of his head. He was not rendered unconscious and had no specific complaints referable to this until about one month later when he noticed a small, slightly tender swelling in the left

FIG. 1 (*left*). Left lateral view of skull, showing circular punched-out defect in frontal bone.
FIG. 2 (*right*). Large bone defect after *en masse* removal of eosinophilic granuloma of left frontal bone.

frontal region, at or near the site of his previous mild injury. The lump seemed to become larger and associated with this were headaches of generalized character. He had no other complaints except for the ringing in his left ear which he had had for some time previously.

Examination. On admission temperature was 98, pulse 76, respirations 18, and blood pressure 140/80. He was a well developed and nourished male, in no acute pain or distress, and did not appear ill. There was a palpable slightly tender swelling in the left frontal region of the skull. General physical examination was completely normal. Neurological examination including cranial nerves, fundi and superficial and deep tendon reflexes was normal. An x-ray of the skull showed in the left frontal region a circular, punched-out, very slightly irregular area of destruction measuring about 2 cm. in diameter. There were no other abnormalities in the skull films. The appearance of the lesion was such as to suggest the possibility of malignancy. Complete survey films of the skeleton were carried out without the finding of any other abnormality. A complete examination of the urological system, including retrograde and intravenous pyelograms, was normal.

Laboratory Data. Red blood cells 4,730,000, hemoglobin 90 per cent, white blood cells 8,600. Differential count: Polymorphonuclears 54, lymphocytes 43, monocytes 1 per cent and eosinophiles 2 per cent. Urinalysis negative. Kahn test negative.

First Operation. On 6 May 1943, under local anesthesia, a complete removal of the tumor

of the left frontal bone was carried out leaving wide margins of normal bone by connecting four burr holes around the site of the tumor. The lesion grossly appeared malignant and it had invaded the dura in three places. A portion of the dura was removed and replaced by a transplant from the temporal fascia.

Course. The patient did well, the wound healed by primary intention, and he was discharged to limited duty about one month later.

Pathological Report. Gross examination: The specimen consists of a rectangular portion of

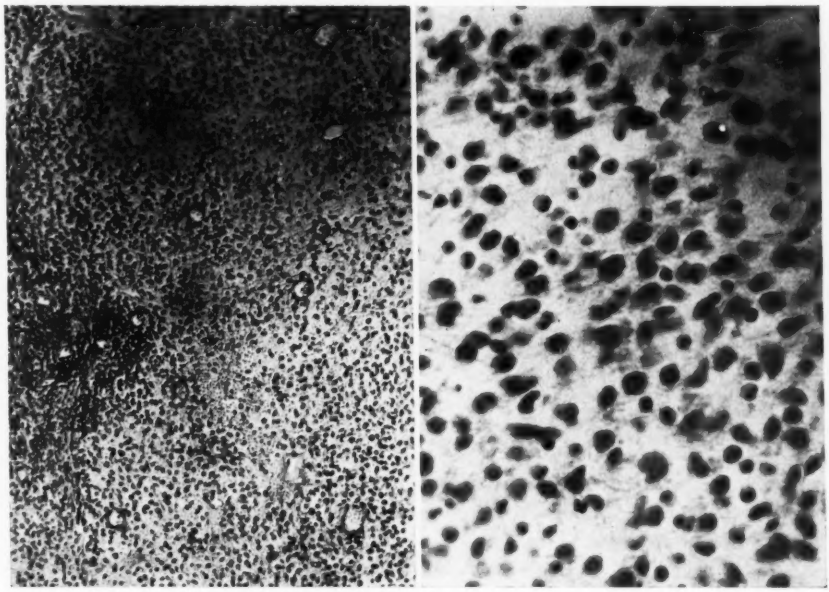


FIG. 3 (*left*). Showing tissue removed from lesion in the skull. There are many large mononuclear phagocytic cells and a predominating number of eosinophiles giving the entire field a reddish appearance. Hematoxylin and eosin (×64).

FIG. 4 (*right*). High-power view of large mononuclear phagocytic cells and eosinophiles. From same field as in Fig. 3 (×320).

skull, 8×8 cm. in size, in the center of which is a circular defect 3 cm. in diameter. The bone here is replaced by a soft red tissue which has infiltrated the overlying galea and has grown through the inner table in a few places, to become adherent to the dura. In the center of the mass is an irregular but roughly circular grey sequestrum 1.5 cm. in diameter.

Microscopical study: Sections show the tissue to consist of a fine fibrous and vascular stroma in which are masses of histiocytes, some appearing as giant cells. The second most prominent feature is the presence of large masses of eosinophiles. There are also scattered lymphocytes, polymorphonuclear leucocytes, and osteoclasts.

Diagnosis: Eosinophilic granuloma of bone.

Interval Note. The patient served on duty in the South Pacific Theater for four months postoperatively on a limited duty status. However, as a result of the skull defect, he had further symptoms of headache and dizziness with unsteadiness and local pain in the region of the defect on excessive activity or on bending over. He was readmitted to the hospital in October 1943, and evacuated to the United States. At a General Hospital in the United States a complete examination was again essentially normal except for the large skull defect in the left

frontal region. Survey films of the skull and of the skeleton showed no evidence of recurrence of the eosinophilic granuloma locally nor of any other similar lesions elsewhere in the body. Laboratory studies were normal as on previous examination and showed no eosinophilia.

Second Operation. On 21 January 1944 the old incision was opened, and the galea dissected away from the dura and from the old fascial transplant over the dural defect. The transplant had functioned apparently as normal dura and there was no evidence of abnormality. The edge of the skull defect was made smooth with rongeurs and the outer table of bone around the entire defect was chiselled away to form a shelf about 2 mm. in width. A piece of tantalum plate was then cut out to fit the defect, made to conform to the contour of the skull in this region of the calvarium, and held in place with triangular pieces of tantalum driven into the bone at an angle over the plate to hold it firmly, according to the method used by Lt. Col. R. Glen Spurling. The wound was closed in two layers with interrupted sutures of #40 cotton.

Course. The wound healed by primary intention and postoperatively the plate presented a very satisfactory cosmetic appearance. The patient was partially relieved of his symptoms of headaches and dizziness and no longer had local pain in the site of the defect on bending over. During his convalescence while playing baseball he fell, striking his head directly over the tantalum plate, but an x-ray showed no change in the position or contour of the plate over that taken during the immediate postoperative period. The patient was discharged to duty about two and one-half months after operation.

SUMMARY

1. Eosinophilic granuloma of bone is a relatively rare condition affecting chiefly children and young adults, usually males.

2. The lesion is benign, may be solitary or multiple, and in more than half of the recorded cases has affected the cranial vault.

3. Although the appearance of the x-ray film of this lesion is suggestive, a diagnosis cannot be made without biopsy and microscopic study.

4. A brief description of the pathology is given with a review of the literature dealing with the intimate pathological relationship of this lesion with Hand-Schueller-Christian disease and Letterer-Siwe disease.

5. The prognosis of eosinophilic granuloma is almost universally favorable. Cases of spontaneous healing have been recorded. Other patients have been apparently cured by surgical extirpation, curettage and by x-ray therapy.

6. One case of this condition occurring in a soldier treated by surgical extirpation in an overseas hospital is presented.

7. A method of covering a skull defect with a tantalum plate is described.

REFERENCES

1. Bass, M. H. Solitary eosinophilic granuloma of bone. *Amer. J. Dis. Child.*, 1941, *61:* 1254–1262.
2. Green, W. T., and Farber, S. "Eosinophilic or solitary granuloma" of bone. *J. Bone Jt. Surg.*, 1942, *24:* 499–526.
3. Jaffe, H. L., and Lichtenstein, L. Eosinophilic granuloma of bone. A condition affecting one, several or many bones, and apparently limited to the skeleton, and representing the mildest clinical expression of the peculiar inflammatory histiocytosis also underlying Letterer-Siwe disease and Schüller-Christian disease. *Arch. Path.*, 1944, *37:* 99–118.
4. Kernwein, G. A., and Queen, F. B. Solitary eosinophilic granuloma. Report of a case. *Surgery*, 1943, *14:* 105–110.
5. Lichtenstein, L., and Jaffe, H. L. Eosinophilic granuloma of bone. *Amer. J. Path.*, 1940, *16:* 595–604.
6. Otani, S., and Ehrlich, J. C. Solitary granuloma of bone, simulating primary neoplasm. *Amer. J. Path.*, 1940, *16:* 479–490.

THE SYMPTOMATOLOGY OF ACOUSTIC TUMORS WITH SPECIAL REFERENCE TO ATYPICAL FEATURES

AXEL OLSEN, M.D., AND GILBERT HORRAX, M.D.

Department of Neurosurgery, The Lahey Clinic, and the New England Deaconess and New England Baptist Hospitals, Boston, Massachusetts

(Received for publication July 26, 1944)

THE SYMPTOMATOLOGY of tumors of the cerebellopontine angle, particularly the acoustic neuromas, has been worked out carefully over a period of many years, beginning with the first case history described by Lévéque-Lasource in 1810.[7] Although this may have been a meningioma, the symptoms were well tabulated. The earliest complete story was that given by Cruveilhier[2] in 1835, in his description of a patient who was proved at autopsy to have a tumor of the eighth cranial nerve. Apparently the first diagnosis of an acoustic neuroma in a living patient was made by Stevens[9] in the United States in 1879. From then until the appearance of the monograph by Cushing[3] in 1917, the reports concerning the clinical syndrome became increasingly frequent.

As summarized by Cushing, the syndrome consisted of a symptomatic progress in the following order:

1. Auditory and labyrinthine disturbances.
2. Occipitofrontal pains and occipital discomfort.
3. Incoordination and instability of cerebellar origin.
4. Evidence of adjacent cranial nerve involvement.
5. Indications of increasing intracranial pressure.
6. Dysarthria and dysphagia.
7. Cerebellar crises and death.

In the majority of cases these symptoms came in this definite chronologic order and the syndrome was verified so often that it was thought to be almost infallible. In fact, we too believe that if the complex is not typical some other type of tumor is likely to be present.

The surgical treatment of these growths has changed radically in the last twenty years, so that the unilateral approach and total removal have become accepted more and more as the best mode of attack. This method was described first by Dandy in 1922[4] and enlarged upon by him in 1934.[5] Accordingly, it becomes obvious that an accurate diagnosis is more than ever essential, especially since a decompressive operation for a nonremovable growth under unilateral exposure has been unsatisfactory. For this reason we examined the histories of the patients seen at the Lahey Clinic from the beginning of the neurosurgical service, November 1, 1932, to January 17, 1942 to determine the reliability of the various symptoms and signs, as well as to gain some idea as to how frequently special methods of examination such as lumbar puncture, special roentgenologic examination and air

studies are necessitated in patients suspected of harboring these tumors.

Our series of verified acoustic neuromas to January 17, 1942 totals 54 patients, but only 42 of these came to the Clinic for their primary operation. Those who had been subjected to previous surgery elsewhere were excluded from this study. The patient's symptoms and signs were considered from the standpoint of subjective and objective manifestations. Obviously, the complete chronologic story rarely is volunteered by the patient and can be obtained only by careful questioning. The chief findings will be discussed as to their frequency, together with their duration before the patient was admitted to the hospital.

SUBJECTIVE DISTURBANCES

Auditory and Labyrinthine. Deafness was present in 39 patients (92.8 per cent), absent in 2, and unknown in 1 because of coma. It was bilateral in 1 patient. The duration of deafness varied from six months to ten years (except in 1 patient in whom it had been present for thirty-two years, probably from other causes). Excluding the thirty-two year case, the average period of deafness was two years and ten months.

With the exception of the 2 cases in which deafness was absent and 4 cases in which it followed tinnitus, deafness was preceded by other symptoms in but 2 patients. In 1 of these, trigeminal disturbances occurred earlier, and in the other, unsteadiness in walking. These 2 exceptions, however, should be borne in mind since they are a definite departure from the almost universal chronology.

Tinnitus was present in 26 patients and absent in 16. It was present on the side of the lesion in 24 instances, bilateral in 1, and on the opposite side in 1. Its duration was from two weeks to over six years. So far as can be judged from the records, tinnitus preceded deafness in only the 4 patients previously mentioned, these two symptoms usually becoming manifest simultaneously. In the 2 patients without deafness, unilateral tinnitus had developed a few weeks prior to their admission.

Perhaps the most striking point about the symptom of tinnitus is that it was absent in 16 patients (38 per cent), whereas it has always been regarded as one of the most frequent and early manifestations of acoustic tumors.

Instability. Thirty-one patients (74 per cent) were aware of staggering or unsteady gait. In 10 cases it was absent, and in 1 case questionable. Only occasionally was it toward the side of the lesion. Instability was one of the earlier symptoms, having been present from two months to three years, with an average for all patients of one year and three months.

Headache. As would be expected, this was a frequent complaint, being present in 34 patients (81 per cent). Its duration was from ten days to ten years, with an average of one year and three and a half months. Excluding the 1 patient in whom headache had been present for ten years, the average was just over one year. In 4 patients headache was said to have antedated all other symptoms, but whether it was due to the tumor is questionable.

Trigeminal Symptoms. Hypesthesia or paresthesia of the face which, with one exception, was on the side of the lesion, was noted by 27 patients, and had been present from five months to five years.

Concerning a possible relationship between headache and pressure upon the trigeminal nerve, it is perhaps noteworthy that all patients without trigeminal symptoms had headache for only a short time or not at all; also, that patients without headache had trigeminal symptoms for six months or less, with one exception in which the duration was three years.

The significance of this observation is not at once apparent. However, it may be inferred that the headache of a patient with an acoustic neuroma is perhaps less significant of increased intracranial pressure than of encroachment on the sensory root of the fifth cranial nerve. This becomes even more possible when analysis shows that in 81 per cent of our cases the duration of the two complaints was relatively similar.

Visual Impairment. Twenty-five patients (59.5 per cent) complained of blurred or double vision. In 14 of these, the complaint had been present for a shorter time than had the headache, and in 10 patients it appeared after the trigeminal symptoms. In 21 cases, the visual symptoms were associated with obvious choked disks or secondary atrophy and blindness. Analysis of the figures fails to show visual symptoms to be any more reliable criteria of increased intracranial pressure than headache, since 13 patients without visual complaints had choked disks and 6 without headache likewise showed papilledema. Four patients with both headache and visual symptoms had no elevation of the optic disks.

Vertigo. This, either constant or in attacks, was conspicuous by its infrequency, being noted in only 13 patients (31 per cent). Its duration was from two weeks to two years.

Subjective complaints related to adjacent cranial nerve involvement, except the fifth, were almost absent. In rare instances dysarthria, dysphagia, squint or facial twitching had been noted by the patient.

OBJECTIVE MANIFESTATIONS

Nystagmus. From the objective standpoint, the only finding uniformly present was nystagmus. This varied in intensity with different patients but could be elicited in all. It was horizontal in every patient and often vertical as well, but whether the excursions differed in rapidity was not noted in all patients. In the 33 cases in which nystagmus was described, there were slower or coarser excursions on deviation of the eyes toward the side of the lesion.

Labyrinthine Impairment. In 9 patients caloric examination of the external auditory canals was not performed, but in the 33 who had this examination there was an absence of response from the labyrinth on the side of the lesion, in 1 patient the loss being bilateral. Of the 2 patients with normal hearing, 1 showed a dead labyrinth on the side of the tumor, and in the other patient the caloric test was not done.

*Impairment of Hearing.** Deafness was present in 39 patients, and could not be determined in 1 because of coma. In 2 of the 39 it was very slight. Two patients had normal hearing bilaterally. The condition was present only on the side of the lesion, except in 1 patient in whom it was bilateral because of chronic otitis media.

Papilledema. In 32 cases the optic disks showed obvious choking, or choking combined with secondary atrophy. The fundi were normal in 8 patients, and in 2 there was questionable edema. In 4 patients pressure on the optic nerves had been allowed to continue for such a long period before they were referred for surgery that they were either blind or had scarcely useful vision at the time of their admission to the hospital.

Trigeminal Involvement. Thirty-three patients had evidence of impaired trigeminal function either as a demonstrable hypesthesia or an absent corneal reflex on the side of the lesion. Seven patients showed no trace of trigeminal involvement, and in 2 it was questionable.

Other Cranial Nerve Involvement. The infrequency of true ocular muscle palsy in cases of acoustic neuroma was noted by Horrax and Buckley,[6] and in in only 4 of our patients was there a definite sixth nerve weakness. Pupillary changes or mild difficulty in conjugate movements, especially upward, were present in 11 other patients. A definite peripheral facial weakness was noted in 12 cases, and a mild or questionable loss was present in 15. Eight patients had evidence of ninth and twelfth nerve involvement, but this was severe in only 2 and questionable in 2 others. Accordingly, it becomes apparent that involvement of the neighboring cranial nerves, except for the fifth, is less common than would be expected, especially when one considers their number and proximity.

Evidences of Incoordination. Unsteadiness in walking was objectively present in 32 patients and absent in 9. Romberg's sign was positive in 26 cases and absent in 15. It was impossible to test 1 patient on account of coma.

Finger-to-nose ataxia was manifested in 38 patients and was not elicited in 4. It was designated as greater on the side of the lesion in 31 patients.

Suboccipital Tenderness. Suboccipital pain or tenderness to pressure or some form of uncomfortable feeling in the back of the head or upper portion of the neck was a fairly common finding, being present in 24 of the 42 patients. It was not of diagnostic value as to the side of the lesion.

VENTRICULOGRAMS

In 8 cases a ventriculogram was considered necessary to determine definitely the need of a suboccipital approach or to differentiate tumor from some other condition. In only 1 patient did the air study lead us to suspect an acoustic neuroma by deformity of the occipital horn of the lateral ventricle, as described by Stone and Schulze.[10] A summary of this case follows:

* In many of the patients hearing tests were made with the audiometer, but in all cases careful tests by the usual clinical methods including air and bone conduction by the tuning fork were carried out, usually by several observers. In the two patients in whom hearing was said to be normal this was so recorded by the audiometer in one patient and in the other the light rubbing of fingers and the faint ticking of a watch could be heard equally well with either ear when the opposite ear was tightly plugged.

Case 1. M. B., a 51-year-old white woman, was admitted to the New England Deaconess Hospital on September 21, 1940, with a complaint of headaches since May 1940. She had had two miscarriages, seasonal hay fever and two minor head injuries in 1939. The headaches were at first occipital in origin with radiation forward, but finally became bitemporal and frontal. They came on suddenly, lasted a few minutes and disappeared as suddenly. During the more severe attacks the patient noticed some blurring of the eyesight. In the summer she began having attacks in which she would suddenly fall to the floor, lose consciousness and jerk her arms a few times. She had no other complaints, but stated that she had been somewhat deaf in the left ear for two years.

General physical examination revealed obesity, normal blood pressure, and negative heart, lungs and abdomen. Pelvic examination showed a large fibroid uterus. There was no scalp tenderness or neck rigidity. Laboratory studies showed a normal blood count and a negative Hinton reaction. There was a faint trace of sugar in the urine on two examinations.

Neurologic examination demonstrated bilateral choked disks and normal pupils. There was nystagmus to the right and left, which was slower on left lateral gaze. There was no facial weakness or hypesthesia. However, there was a slight left-sided deafness. Regrettably, caloric studies were not done. The deep reflexes were a little more active on the left. There was no ataxia, but on trying finger-to-thumb approximation, she was a little slower on the left than on the right. A moderate degree of generalized hypotonia was also noted.

It was felt that she was suffering from an intracranial tumor, probably midline cerebellar in location, but the signs were too few to warrant surgery without an air study. A lumbar puncture was not done because of papilledema.

On September 23, a ventriculogram was made and this showed uniformly dilated lateral and third ventricles, but there was a slight elevation of the left occipital horn. The third ventricle was also shifted to the right and slightly superiorly at its posterior end. These changes were thought to be sufficient to warrant a left suboccipital exploration for an acoustic neuroma. This was performed the same day and what was described as a moderate-sized tumor was removed completely without difficulty.

The postoperative course was amazingly uneventful and she was discharged on October 16, moderately ataxic on the left side but able to be up and about. She had the usual complete facial paralysis but refused an anastomosis at that time. On May 5, 1941, she returned and a hypoglossal-facial anastomosis was performed. There was at this time a moderate-sized collection of fluid under the scalp flap which was aspirated. She stated that this became somewhat tense at times but that she felt well and was doing her housework.

Comment. In retrospect it is obvious that not sufficient attention was placed upon the slight but definite deafness of the left ear, probably because there was no accompanying trigeminal hypesthesia. Caloric examinations doubtless were omitted because the deafness was so slight, but in all certainty they would have shown a dead labyrinth on the left. This, of course, would have clinched the diagnosis. It is probable too that if a lumbar puncture had been performed, and this had disclosed an elevated protein content of the spinal fluid, the patient might have been spared the ventricular study. However, the usefulness of this procedure in occasional somewhat obscure cases must always be considered.

In a second case in which ventriculography was utilized, evidence of a posterior fossa tumor was definite from air study, but an acoustic neuroma was not expected. The following case is representative:

Case 2. V. S., a 37-year-old white woman, was admitted to the New England Deaconess Hospital on April 5, 1937, with the complaint of headaches for four years and dizziness and double vision for one year. The family and marital history were negative. She had had a toxemia of pregnancy many years before and a minor head injury three years previously.

The headaches were of two kinds. The first type came on when she lifted her head while lying down and was a dull ache of short duration, appearing in the right suboccipital region. The other type came on about once a month and was a sharp prostrating pain appearing like two prongs, starting in the back of the head and radiating forward on each side.

One year before admission, she noticed staggering when she walked, with a tendency to deviate to the left, and some clumsiness of the left hand. Two months later she developed double vision and four months later a dull ringing noise in the right ear. Four months preceding admission she noticed some flashes of pain in the right cheek and recently some tingling on both sides of the mouth.

General physical examination showed an apprehensive patient with no abnormalities noted in the mouth, throat, lungs, abdomen or genito-urinary tract. Routine blood and urine examinations were normal.

Neurologic examination revealed chronic, bilateral choked disks but normal visual acuity. There was nystagmus to the right and left, with slower excursions on left lateral gaze. There was slight hypesthesia of the left side of the face but no facial weakness and no loss of hearing. Caloric examination was not made. The lower groups of nerves were normal in activity on both sides. There was ataxia of the left arm and leg on doing the various tests. There was a positive Romberg's sign, and the gait was ataxic with deviation usually to the left. Deep reflexes were overactive throughout but were equal.

The impression was that this patient was suffering from a midline cerebellar or a posterior third ventricle tumor. On April 8, 1937, a ventriculogram showed uniformly dilated lateral and third ventricles. On bilateral suboccipital exploration the same day, a left acoustic neuroma was exposed and removed completely. It was felt that the facial nerve was preserved during the removal and this has subsequently proved to be correct. The growth itself was of only moderate size, but there was a large arachnoid cyst overlying it.

After an uneventful postoperative course, she was discharged on May 1 in good condition and with a little motion beginning to appear in the left side of the face.

Comment. This case again represents the importance which would doubtless have been placed upon an absent labyrinthine response if a caloric examination had been performed. It was probably omitted because the patient had no deafness, a fact which in itself militated against the diagnosis of an acoustic tumor. However, it is the occasional departure from the usual that needs emphasis, and obviously when patients, like this one, have even a slight trigeminal involvement along with cerebellar symptoms, tests of labyrinthine function should certainly be a part of the examination.

ROENTGENOGRAMS

There was no case in which roentgenologic examination of the petrous ridges or of the internal auditory meati was the final diagnostic criterion, but the roentgenograms showed positive findings in 9 of the 15 cases in which they were made. The examinations used were first described by Carr in 1917[1] and Towne in 1926.[11]

LUMBAR PUNCTURE

In our opinion, "routine" lumbar punctures in patients harboring intracranial tumors are not only contraindicated but are definitely dangerous, particularly so when there is a lesion in the posterior fossa because of greater herniation of the cerebellar tonsils through the foramen magnum. However, in certain instances the spinal fluid findings may be of distinct diagnostic aid, and if the procedure is carried out in a hospital where imme-

diate operative intervention can be instituted if necessary, the danger is at least greatly minimized.

In two of our patients lumbar puncture contributed distinctly to the correct diagnosis. One of these cases is summarized here. In a third patient, a spinal puncture done elsewhere precipitated a train of symptoms which a few days later was diagnostic of an acoustic neuroma. Merritt[8] has stated that acoustic neuromas, of all the brain tumors, are most prone to produce elevation of the protein content of the fluid obtained by lumbar puncture. Nine of our patients had the procedure performed here or elsewhere, and all showed proteins of 100 mg. per cent or more. In the following case the protein elevation gave us the final clue between an acoustic neuroma and an intrapontine lesion.

Case 3. L. S., a 63-year-old white woman, was admitted to the New England Deaconess Hospital on March 18, 1940, with a complaint of numbness in the left side of the face and decreased hearing in the left ear for one year. At the onset of the trouble she noticed some noises in the left ear, but these stopped after a time. The deafness and numbness had slowly progressed. At the time of menopause, fifteen years before, she had a great deal of nervousness and this had recurred and become very severe in the month before she was admitted. She had had sick headaches when younger but none for thirteen years. In the last three years she had had frontal headaches and a feeling of fullness around the left eye which went away when she was busy with housework. She had had teeth extracted for the facial trouble, and a fairly severe anemia developed which was relieved by treatment. The remainder of the history was not significant.

General physical examination showed dehydration, evidence of weight loss and peripheral arteriosclerosis. The blood pressure was 148 mm. of mercury systolic and 90 mm. of mercury diastolic. Laboratory studies revealed a trace of sugar in the urine, the red blood cell count was 4,910,000, the white count 8,950, and the hemoglobin 101 per cent. The blood Hinton was negative. A roentgenogram of the skull revealed calcification in both internal carotid arteries.

Neurologic examination showed mild mental confusion, memory loss, poor insight and orientation. The optic disks were blurred nasally and the pupils were unequal, the left being larger than the right, but both reacted well. Nystagmus, horizontal in direction, was present both on looking to the right and left, but was slower and of wider excursion on left lateral gaze. There was definite hypesthesia in all three divisions of the left fifth nerve, most pronounced in the third. A slight left peripheral facial weakness was present as well as a mild right central one. The left ear was deaf, and the caloric response was absent on that side. The other cranial nerves were negative, and there was no localized weakness of the extremities or sensory change. Deep reflexes were active throughout but a little more so on the right and the superficial reflexes were not significant. Coordination tests revealed a little ataxia on the left, an unsteady gait and a tendency to fall backward in the Romberg position.

It was our impression that the patient was suffering from an intrapontine or left cerebellopontine angle tumor in addition to cerebral arteriosclerosis. Lumbar puncture revealed a pressure of 100 mm. of water and xanthochromic fluid containing 480 mg. of total protein per 100 cc. Reexamination of the roentgenograms showed erosion of the medial end of the left petrous ridge.

With these findings a diagnosis of left acoustic neuroma was made. On March 27, 1940, a left unilateral suboccipital craniotomy was performed and a moderate-sized acoustic tumor was removed completely without difficulty. The internal auditory meatus was curetted and the facial nerve sacrificed.

The postoperative recovery was slow, chiefly because her mental status remained unimproved and she refused to eat. She also developed cystitis due to total incontinence. She was discharged in fair condition on May 17. The left eyelid was closed permanently by suture on September 18, 1940, in order to take care of a severe keratitis and at this time her mental status was still only slightly improved.

SUMMARY

Although the specific symptomatology and particularly the chronologic development of symptoms is highly important in the diagnosis of acoustic tumors, nevertheless the occasional absence of certain usual features, especially deafness, should be emphasized.

The subjective symptoms and objective findings in a series of 42 patients having verified acoustic neuromas have been analyzed. The usual chronology of the patient's complaints in this series is in essential agreement with the summary given by Cushing in his monograph in 1917. Certain features, however, bear emphasis. Tinnitus, for instance, was absent in 38 per cent of patients, and although it was noticed usually at about the same time as impairment of hearing, it preceded deafness in only 4 instances. The close association of trigeminal nerve involvement with headache was of interest, and it may be that headache in a patient with an acoustic tumor is less significant of increased intracranial pressure than of pressure upon the fifth cranial nerve. This is further borne out by the fact that 4 patients who had both headache and visual symptoms showed no papilledema.

One significant objective observation was the presence of nystagmus in every patient. It was slower toward the side of the lesion in all instances in which it was recorded.

Caloric examinations were omitted in 9 patients, but an absent response from the labyrinth on the side of the lesion was ascertained in every case in which the test was carried out. The value of an absent response from one side as diagnostic of an acoustic growth in patients having cerebellar signs and symptoms hardly can be overemphasized. Caloric tests should always be performed whenever there is the slightest suspicion of an acoustic neuroma, and not infrequently may obviate the necessity of a ventriculogram in doubtful cases. The latter, however, may still be necessary in rare instances, and the same is true of a diagnostic lumbar puncture.

REFERENCES

1. Carr, G. L. Roentgen ray findings in the skull in cases of brain tumors, with special reference to the porus acusticus. *Amer. J. Roentgenol.*, 1917, *4:* 405–410.
2. Cruveilhier, J. Cited by Cushing[3] (p. 4).
3. Cushing, H. Tumors of the nervus acusticus and the syndrome of the cerebellopontile angle. *Philadelphia & London: W. B. Saunders Co.*, 1917, 296 pp. (p. 176).
4. Dandy, W. E. An operation for the total extirpation of tumors in the cerebello-pontile angle. A preliminary report. *Johns Hopk. Hosp. Bull.*, 1922, *33:* 344–345.
5. Dandy, W. E. Removal of cerebellopontile (acoustic) tumors through a unilateral approach. *Arch. Surg., Chicago*, 1934, *29:* 337–344.
6. Horrax, G., and Buckley, R. C. A clinical study of the differentiation of certain pontile tumors from acoustic tumors. *Arch. Neurol. Psychiat., Chicago*, 1930, *24:* 1217–1230.
7. Lévêque-Lasource, A. Cited by Cushing[3] (p. 3).
8. Merritt, H. H. Cerebrospinal fluid in cases of tumors of the brain. *Arch. Neurol. Psychiat., Chicago*, 1935, *34:* 1175–1187.
9. Stevens, G. Cited by Cushing[3] (p. 10).
10. Stone, R. S., and Schulze, F. J. Ventricular changes caused by proved tumors of the brain. *Amer. J. Roentgenol.*, 1938, *39:* 523–533.
11. Towne, E. B. Erosion of the petrous bone by acoustic nerve tumor. Demonstration by roentgen ray. *Arch. Otolaryng., Chicago*, 1926, *4:* 515–519.

POST-TRAUMATIC HEADACHE*

CHARLES BRENNER, M.D., ARNOLD P. FRIEDMAN, M.D., H. HOUSTON MERRITT, M.D., AND D. E. DENNY-BROWN, M.B.

The Neurological Unit, Boston City Hospital, and the Department of Neurology, Harvard Medical School, Boston, Massachusetts

(Received for publication July 27, 1944)

INTRODUCTION

HEADACHE, dizziness, difficulty in concentration, nervousness and insomnia, are common after-effects of head injury, and the frequent association of all these symptoms forms the clinical entity described as the "post-traumatic syndrome." Of this group headache is probably the most important symptom and may appear singly as well as in combination with the others.

The incidence of headaches following head injuries varies in the reports of different observers—Guttmann[4] found it in more than 50 per cent of the cases; Russell[11] 42 per cent; Penfield[8] 33 per cent, persisting more than six months in 28 per cent; Rowbotham[10] in 80 per cent, while Knoflach and Scholl[5] state that mild headaches occur after every head injury. Some of the discrepancies among the various investigators may be explained by the selection of the cases studied, complications following injury, variations in length of follow-up, and type of therapy used.

Considerable difference of opinion exists as to which are the most important factors in the causation of post-traumatic headaches. Schaller[12] lists headache as a symptom of post-traumatic psychoneurotic state and not under post-traumatic concussion state (encephalopathy). Woltman[14] feels that such an explanation is unlikely because of the regularity with which headaches appear. Bremer et al.[1] regard vasomotor instability as an important factor in post-traumatic headache. Penfield and Norcross[8] state that meningeal adhesions may be responsible for the headaches. Rowbotham[10] expresses the opinion that many of the symptoms of the post-concussional syndrome, such as headache and dizziness, have a direct organic basis. One of the authors,[2] discussing the sequelae of war head injury, emphasized the importance of recognizing both physical and emotional trauma as associated factors. Attention was called to the occurrence of headache after very mild as well as very severe head injury. Symonds[13] also says that physiogenic and psychogenic factors are so closely interwoven when there is organic cerebral damage that a separation between them is unnatural and the practice of dividing cases of post-concussional syndrome into two groups, labeling the syndrome organic in one and functional in the other, is unprofitable and misleading. Lewis[6] is in agreement with Symonds.

In summarizing the views of the various authors it appears that there

* The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the President and Fellows of Harvard College.

are essentially three opinions. Some authors relate post-traumatic headache (as well as the other symptoms of the post-traumatic syndrome) exclusively to psychological factors, some exclusively to physiological ones, and some emphasize the importance of both types of factors in the great majority of cases.

As emphasized by one of us[2] it is evident that the complaints of the patient following head injury will vary not only with the manner and degree of injury but with the personality structure of the patient, compensation factors, and his environmental status. The purpose of this investigation was to study the interrelation of such factors with particular reference to the symptom of post-traumatic headache in a group of civilian head injuries admitted to a general hospital.

METHOD

The present report is based on a series of 200 consecutive head injuries admitted to the Boston City Hospital. Selection to some extent was inevitable, for the requirements of the inquiry necessitated that cases be excluded if the essential data on duration of loss of consciousness were lacking because of alcoholic stupor or other unrelated complications. Further, since the main objective of the inquiry was related to disability in healthy persons in regular occupations, the study was limited to age groups between 15 and 55 years and excluded chronic alcoholics and chronic unemployed. The material, selected in these respects, was fairly evenly distributed in the age group 15 to 54, and consisted of 125 males and 75 females of a variety of national stocks (71 predominantly Irish) and occupations (96 skilled or semi-skilled workers).

The patients were first examined as soon as they were brought into the hospital, which in most cases was within a few hours after the accident. They then were followed daily during their hospital stay and at intervals of one to two months for periods of six to fifteen months in the out-patient clinic. On each follow-up visit each patient was seen by a neurologist, psychiatrist, psychometrist, electroencephalographer, and social service worker. Roentgenograms, spinal fluid examinations, electroencephalograms and other laboratory procedures were done when possible during the hospital stay and on some patients in the course of the follow-up. Whenever possible, the following factors concerning the patient were especially noted: type of accident, location of any scalp or skull injury, and extent and location of any brain injury. During the hospital course the following things were ascertained about the headache: its location, type, mode of onset, when first experienced, effect of posture, sleep, mental and physical effort, and lumbar puncture. The associated symptoms and signs were noted, what relieved and what aggravated the headache, the duration and frequency of the attacks, and the affective state of the patient. During convalescence a similar procedure was followed, with further investigation of any previous history of liability to headache and any family history of headaches. In all possible cases examinations of vision, ear, nose, throat, etc. were done to make sure that there were no extraneous factors that might be causing the headache.

RESULTS

Post-traumatic headaches occurring in our patients were characteristically intermittent, lasting usually a few hours, though the duration varied from a few minutes to several days. They were variable in severity and were described by the patients as steady, throbbing, aching, dull, burning, or pressing. They were generalized, sharply localized, or polar (e.g. bifrontal, bioccipital). The most common precipitating factors were sudden change in posture, fatigue or effort, and emotional upsets, though the group

in which the headache was unrelated to any known factor was as large as any of these. They were usually relieved by rest, quiet, and the ordinary analgesic drugs. They rarely lasted overnight. Headaches occurring immediately after injury in our series conformed to this very broad description as well as those occurring later in convalescence with the single exception that the former were more apt to last continuously for one to several days.

One hundred thirty-eight (69 per cent) of the 200 patients had headache at some time during their post-traumatic course. For purposes of discussion we have divided the cases into several groups. The first group comprises 123 patients (62 per cent) who complained of headache while still in the hospital. The second group consists of 81 patients (41 per cent) who complained of headache at any time after leaving the hospital. It will be noted that these two groups overlap. The second group was subdivided into those patients (18 or 9 per cent) whose headaches stopped within two months of the time of injury and those (63 or 32 per cent) whose headaches persisted for longer than two months after injury. We have selected the period of two months as a reasonably satisfactory, though obviously arbitrary, line of division since certain patho-physiological reactions such as bleeding, bruising, edema, etc. have presumably subsided by that time. In addition there is the added consideration of the practical problem presented by the patient whose headaches persist for a period longer than two months. The two other groups of patients that were also studied were one of 59 patients (30 per cent) who complained of headache while in the hospital, but had none after discharge, and the group of 11 patients (6 per cent) whose headaches did not begin until after hospital discharge.

In analyzing our data we have correlated various factors of presumed or possible significance in the case records with (1) the incidence of headaches lasting longer than two months after the injury (post-traumatic syndrome), (2) the type of headache complained of (localized unilateral, localized polar, or generalized), (3) the relationship of the headache to the precipitating factors mentioned above, and (4) the incidence of headache immediately after the injury during the hospital stay.

POST-TRAUMATIC HEADACHES LASTING LONGER THAN TWO MONTHS AFTER INJURY

A. *Correlation with Psychiatric Evaluation and Factors Indicative of Psychological Reaction to Injury* (Table 1). The incidence of headache lasting longer than two months after injury was significantly high in the following groups of patients. (1) Those patients who were considered to have been neurotic or generally nervous prior to the accident. (2) Those patients who, without disturbance of consciousness, exhibited restlessness, excitability, apathy, or particularly any severe emotional reaction during the first week after the injury. (3) Those patients who after discharge complained of fears, anxieties, fatigability, nervousness, irritability, or inability to concentrate. (4) Those patients with complicating environmental factors that might con-

ceivably increase their emotional strain. Of these factors, occupational difficulties and pending litigation seemed to be of the greatest significance. It may be mentioned that patients considered to be psychopathic personalities showed an average incidence of prolonged post-traumatic headache.

B. *Correlation with Factors Related to Severity of Injury* (Table 2). The incidence of post-traumatic headache lasting longer than two months was significantly low in the following groups of patients. (1) Those who had no

TABLE 1

Correlation between duration of headache and factors related to mental reaction to head injury

	Duration of Headache					
	None		Less than 2 months		More than 2 months	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Pre-Traumatic Psychiatric Evaluation						
Normal	54	61	9	10	26	29
Neurotic or nervous	12	45	2	7	13	48
Psychopathic personality	21	61	2	6	11	33
Immediate Post-Traumatic Mental Reaction						
None	81	62	16	12	35	26
Clear with reactions of apathy or excitability, restlessness or severe emotional reaction	19	44	2	5	22	51
Late Post-Traumatic Mental Reaction						
None	104	80	13	10	13	10
Fears, anxieties, fatigue, inability to concentrate, nervousness, irritability	10	17	5	8	44	75
Complicating Environmental Factors						
None	60	83	7	10	5	7
Pending litigation	10	29	3	9	21	62
Occupational difficulties	2	20	2	20	7	60

disturbance of consciousness or were only dazed as a result of the injury. (2) Those who were not disoriented following the injury. (3) Those who suffered no post-traumatic amnesia as a result of the injury. It should be noted, however, that there was no correlation between the *duration* of coma, disorientation, or post-traumatic amnesia, when these were present to a measurable degree, and the incidence of prolonged headache. On the other hand, the incidence of prolonged headache was significantly high in the group of patients with laceration of the scalp. Of the 7 patients who suffered from prolonged headache and were not unconscious in the initial injury, 5 had had a scalp laceration.

There was suggestive evidence of increased incidence of prolonged headache in those patients who exhibited on mental test diminution in intellectual ability attributable to head injury, whether within the first twenty-four hours or later during hospital stay.

TABLE 2

Correlation between duration of headache and factors related to severity of injury

	Duration of Headache					
	None		Less than 2 months		More than 2 months	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Duration of Coma						
None or dazed	14	70	4	20	2	10
Less than 10 minutes	50	56	8	9	32	35
10 to 60 minutes	37	60	5	8	20	32
More than 1 hour	15	66	1	4	7	30
Duration of Disorientation						
None	11	61	5	28	2	11
Less than 1 hour	50	53	8	9	35	38
1 to 12 hours	41	67	5	8	16	25
More than 12 hours	17	63	0	0	10	37
Post-Traumatic Amnesia						
None	11	65	5	29	1	6
Less than 1 hour	56	55	8	8	37	37
1 to 12 hours	34	63	5	9	15	28
More than 12 hours	17	63	0	0	10	37
Scalp Laceration						
None, or scalp bruise or abrasion	76	64	14	12	29	24
Scalp laceration	40	53	4	5	31	42

There was no correlation between incidence of prolonged headache and the following factors: Generalized electroencephalographic abnormality during first week after injury, reflex changes due to injury, increased cerebrospinal fluid pressure, presence of blood in the cerebrospinal fluid on first or subsequent lumbar puncture, presence of signs of skull fracture, or duration of hospital stay. The number of patients with extracerebral hematomas, with convulsions, or with intellectual deficit at the time of the first follow-up visit was too small to permit of statistical treatment.

C. *Miscellaneous Correlations* (Table 3). The incidence of prolonged headache did not differ from average in the group of 12 hypertensive patients and the 10 patients with cranial operations, indicating that the inclusion of these groups did not influence the validity of our results. There was good correla-

tion between the duration of dizziness and the duration of headache, substantiating the well known association of these two symptoms in the post-traumatic syndrome. There was a strikingly low incidence of prolonged headache in the group of patients who were able to return to work within 7 days of injury and a strikingly high incidence in the group who were incapacitated for longer than six months. There was also a strikingly low incidence

TABLE 3

Correlation between duration of headache and miscellaneous factors

	Duration of Headache					
	None		Less than 2 months		More than 2 months	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Place or Type of Accident						
Industrial	11	45	3	12	10	43
Recreational	9	75	2	17	1	8
Domestic	11	73	2	13	2	14
Fighting or Robbery	17	71	1	4	6	25
Traffic	48	53	9	10	34	37
Street	13	81	0	0	3	19
Time off Work						
Less than 7 days	38	91	3	7	1	2
Less than 1 month	42	59	7	10	22	31
Less than 2 months	8	35	3	13	12	52
2 to 6 months	9	45	2	10	9	45
Over 6 months	2	14	0	0	12	86
Duration of Dizziness						
None	103	78	9	7	20	15
Less than 2 months	9	41	7	32	6	27
2 to 6 months	5	33	1	7	9	60
Over 6 months	2	6	1	4	28	90

of prolonged headache in the group of recreational accidents, a suggestively low incidence among domestic accidents, and a suggestively high incidence among industrial accidents. The incidence of prolonged headache did not correlate significantly with age, sex, occupation, manner of injury, schooling, or intelligence.

There were 11 patients with headaches that lasted longer than two months after injury but which did not begin until after hospital discharge. In 7 of these 11 patients the headaches began within one week after discharge and in the other 4 at a later date. The size of this group is too small to permit of significant generalizations, but it might be of interest to mention that in the 4 patients with late onset of headache the precipitating factors were emotional in three and fatigue in one.

LOCALIZATION OF HEADACHE

Eighty-one patients complained of headache after hospital discharge. One of these was discarded because of insufficient data. Of the remaining 80 patients, 28 (35 per cent) had generalized headaches, 36 (45 per cent) had localized polar headaches (i.e. bifrontal, bitemporal, biparietal, or bioccipital) and 16 (20 per cent) had localized unilateral headaches. The incidence of each of these three types of headache was correlated with the psychiatric evaluation and factors related to psychological reaction to injury, with factors related to the severity of the injury itself, and with most of the miscellaneous factors mentioned above. No statistically significant correlations were found.

Special attention was paid to the relationship of localized headache (both polar and unilateral) to localized scalp or skull injury. Of the 52 patients with localized headache, in 20 (38 per cent) the site of the headache coincided with that of scalp or skull injury, and in 17 (33 per cent), of which 3 had unilateral and 14 polar headaches, there was no evidence of localized scalp or skull injury. Of the remaining 15 cases, 1 had multiple scalp lacerations with headache localized to one laceration only, 1 had multiple headaches, one of which coincided with a scalp laceration, 2 had very long lacerations with headache localized to a part of the laceration, 3 had evidence of contrecoup injury with headache localized to the region of the contrecoup, and 1 case was discarded because the data were considered to be unreliable. There remain 7 cases in which localized scalp or skull injuries were present but the headaches were localized elsewhere in the head.

RELATIONSHIP TO POSTURE, FATIGUE OR EFFORT, AND EMOTIONAL UPSETS

Though other precipitating factors were considered in relation to post-traumatic headache, the three mentioned in the heading above were the only ones present in any substantial number. Relation to posture was noted in 25 cases, to effort or fatigue in 22 cases, and to emotional upset in 11 cases, while there was no observed relationship of headache to other factors in 19 cases. Correlations were carried out with the same factors as in the two previous sections. The only clearly significant correlation obtained was that 10 of the 11 patients whose headaches were related to emotional upsets also complained of post-traumatic fears, anxieties, nervousness, etc. In the group related to posture 15 of 25 complained of such anxiety symptoms. Postural headaches were not more common after prolonged disorientation or initial subarachnoid hemorrhage than were headaches provoked by effort or by emotion or by no particular factor. There was no correlation between presence of vascular hypertension and any of the precipitating factors considered in this section.

HEADACHE DURING HOSPITAL STAY

One hundred twenty-three patients (62 per cent) complained of headache during hospital stay. The incidence of such headaches was correlated with

the same factors as in the two previous sections. The only statistically significant correlation was that the incidence of headache in the hospital was lower in the group of confused patients than in the group without confusion, regardless of the type or degree of emotional reaction to the injury. There was no evidence of high incidence of headache in the hospital associated with ingestion of alcohol at time of injury or with hypertension, indicating that these two complicating factors did not vitiate the results.

The group of 59 patients who had headaches while in the hospital but complained of none after discharge was compared with the group of 63 patients whose headaches lasted for two or more months after the time of injury in an effort to determine whether there were any characteristic differences between the two groups. The most striking difference was the positive correlation between the incidence of post-traumatic fears, anxieties, etc. and prolonged post-traumatic headache, and the negative correlation between the incidence of such post-traumatic symptoms and that of headaches not lasting beyond hospital stay (brief headaches). Otherwise there were no clear statistical differences to be observed although there was a suggestively higher incidence of brief headaches among those patients with very mild head injury (no measurable coma, disorientation, or post-traumatic amnesia), and a suggestively higher incidence of prolonged headache among those patients with skull fractures and those who were considered to have been nervous or neurotic before the time of injury. However, there are notable exceptions. For example, one patient who had a post-traumatic amnesia of over fourteen days, a bloody cerebrospinal fluid, and a hospital stay of almost four months had no post-traumatic headache, while a patient with a very slight injury and a post-traumatic amnesia of only a few seconds had headache of six months' duration.

HEADACHE LOCALIZED TO REGION OF KNOWN DAMAGE TO SCALP OR SKULL

It might be supposed that, whatever the pathogenesis of generalized types of headache, those localized to known areas of contusion or laceration of scalp with or without fracture of skull could be regarded as a control group with similar mechanism. There were 20 such cases in this series, in 11 of which the headache was localized unilaterally, 9 polar. In 6 of them the headache was related to posture, in 9 to effort, in 1 to emotional disturbance, in 1 to sleep, and in 3 to no known association. The headache began during hospital stay in all but one case, and had subsided within 2 months in 8. In 11 the headache lasted over 6 months, and in 7 of these over 9 months.

These 20 examples of headache localized to a known scalp or skull injury presented correlations with other factors closely resembling the whole group. Sixty-five per cent had been disoriented for less than 60 minutes (25 per cent dazed or no loss of consciousness), only 3 of the patients had abnormal reflex signs in hospital, 4 had bloody spinal fluid and only 1 had a

localized change in E.E.G. A positive pre-traumatic psychiatric history was obtained in 11, and post-traumatic mental symptoms occurred in 10 (50 per cent). There was correlation with complicating environmental factors in 12 (litigation in 4). Twelve patients returned to work within 2 months, 4 more within 6 months. Such headaches therefore did not prove to be exceptions to the general average. Only 2 of this group had required operative treatment, and none developed complications. The outstanding differentiating correlation was the large part played by posture and effort in provocation of headache during convalescence.

DISCUSSION

The Post-Traumatic Syndrome. The high degree of correlation between the incidence of prolonged headache and the incidence of post-traumatic nervous reactions (fears, anxieties, nervousness, fatigue, and inability to concentrate) as well as of prolonged dizziness is, of course, merely a statistical validation of the concept of post-traumatic syndrome that has been so frequently described in the literature. That this syndrome is often associated with prolonged occupational disability is also well known and this fact too is borne out by our results.

We have found no evidence to differentiate headache when it occurs as an isolated symptom from headache as part of the post-traumatic syndrome.

The results of our statistical correlations indicate, however, that it is erroneous to consider post-traumatic headache merely as an expression of "compensation neurosis," for the identical headache, associated with anxiety, correlated equally well with domestic or occupational worry uncomplicated by the possibility of compensation. In a certain group of patients the symptoms continued after work had been resumed or compensation had been settled. The high incidence of headache in a group of 100 cases without loss of consciousness as compared with a similar group with loss of consciousness found by Schaller[12] is reversed in our series, when loss of consciousness was objectively observed and recorded in detail. We therefore find no evidence to support the subdivision "post-traumatic psychoneurotic state" and "post-traumatic concussion state" proposed by him.

In the present group of patients we have been able to demonstrate a high incidence of prolonged headaches among those patients who were considered to have been nervous or neurotic prior to the accident, among those with complicating environmental factors (including compensation) likely to produce emotional stress, and among those with symptoms of a marked, immediate emotional reaction to the injury, as well as a low incidence of such headaches among patients who were injured at play. These correlations indicate the importance of emotional and environmental stress in the causation of post-traumatic headaches. No single type of stress emerged as a factor of paramount importance.

On the other hand we have also demonstrated a strikingly low incidence

of prolonged headaches among those patients with very mild head injuries (no measurable duration of coma, disorientation, or post-traumatic amnesia), and a high incidence among patients with scalp lacerations. These correlations indicate that the severity of the physical injury plays some part as well as the degree of emotional and environmental stress.

The phrase "severity of physical injury" here requires closer examination. It will be noted that the factors which might be supposed to reflect the degree of traumatic intracranial damage, namely increased intracranial pressure or the presence of blood in the spinal fluid immediately after injury, or electroencephalographic abnormality at any stage, were not significantly related to subsequent liability to headache. The presence of coma, disorientation and amnesia held a positive correlation but not the relative duration of these. It is therefore doubtful if the *degree* of brain or meningeal injury is of significance in the genesis of headache. This also applies to the few cases in which a change in ventricular shape was demonstrable by air encephalogram, of which the only two examples that were studied remained free from headache. Headache is related in some way with the fact of injury but not with any given feature of pathology demonstrable with the methods used. The 17 instances of absence of coma or disorientation were in fact remarkably free from post-traumatic symptoms of any kind. Only 3 of this group developed psychoneurotic symptoms and only 1 remained away from full work for longer than 2 months.

Statements have appeared in the literature (Russell[11]) to the effect that the type of headache present in the post-traumatic syndrome is relatively uniform. In our series this was decidedly not the case. There was no correlation between the incidence of prolonged headache and type of headache (localized unilateral, polar, or generalized), nor the relationship of the headache to posture, fatigue, or effort. The headaches encountered were in fact of any type, and of variable severity, duration, and frequency.

Of the various kinds of headache encountered those related to change in posture and those localized to a region of the head known to have been lacerated in the original injury would appear *a priori* to have the greatest likelihood of underlying structural disorder. It was therefore surprising to find that patients who complained of posture, or change of posture, as a precipitating factor had as a group no particular evidence of type or severity of injury and had a high correlation with psychiatric symptoms. This latter point loses some significance, however, when it can be stated that *all* physical symptoms had a high correlation with mental symptoms. Thus of patients without headache in convalescence only 9 per cent complained of mental symptoms (anxiety, fatigue, nervousness, or change in mood), 72 per cent of those whose headaches were related to posture complained of such symptoms, 73 per cent of those with headache related to effort, and 91 per cent of those who described emotion as a precipitating factor. Headache localized to the point of scalp injury also failed to correlate with any specific evidence of

type or severity of injury, though the high proportion of these produced by posture or effort reinforces the suspicion of structural change underlying such precipitation.

Localized headaches have a further particularly interesting feature in their sensitivity to the effect of histamine, as described by Friedman and Brenner.[3] A series of 20 patients with localized post-traumatic headaches who were given intravenous histamine were studied. In 13 of the cases the headache produced by the injection of histamine was identical in character and location with the post-traumatic headaches of which the patient complained, and in 3 other cases it was strikingly similar to them. These results suggest that in a certain group of patients with post-traumatic headaches, the pain sensation of the headaches involves structures affected by histamine. The essential element of histamine headache in the normal individual as elucidated by Pickering[9] and Northfield[7] is the painful distention of the arteries around the brain. Histamine does not reproduce localized headache in a person subject to migraine. The reproduction of localized, particularly unilateral, post-traumatic headache by histamine implies the existence of a localized vascular sensitivity resulting from the injury. We have not determined the longest period of persistence of such effects, though we have found it present 12 to 14 months after head injury. Such an hypothesis for the mechanism of post-traumatic headaches affords a possible reasonable explanation for the association of the headaches with both physical and emotional factors. In the former case one assumes that the circulatory changes due to postural changes or physical effort distend the vessels previously sensitized by the head trauma, while in the latter case the same distention would be assumed to result from the well known circulatory changes incident to emotional reactions. It is not, of course, implied that all post-traumatic headaches have this mechanism. Only when the headache is localized and lateralized is the histamine reaction convincing. As has been stated above we have not succeeded in finding any significant differences between the correlations and the various factors examined in such cases and in other types of headache. Other means of differentiation have yet to be discovered. Finally, it should be stated that when the whole group of patients with persistent headache in convalescence was compared with the group of nearly equal size with headaches that did not persist beyond the hospital stay the comparison yielded no positive results. The correlations with the various factors indicative of severity of injury, the pre-traumatic psychiatric evaluation, and the immediate psychological reaction to the injury yielded essentially the same values for the two groups.

SUMMARY

1. Two hundred consecutive hospitalized cases of head injury between the ages of 15 and 55 years, exclusive of chronic alcoholism and vagrants, were followed from the time of injury for a period of six or more months.

The investigating team consisted of neurologists, psychiatrists, psychometrist, electroencephalographer, and social worker.

2. One hundred thirty-eight patients (69 per cent) complained of post-traumatic headaches, 63 patients (32 per cent) of headaches lasting longer than two months, and 59 patients (30 per cent), of headaches that did not persist beyond the hospital stay. In 11 patients (6 per cent) the headaches began after discharge from the hospital.

3. Post-traumatic headaches are regularly intermittent. They may be precipitated by postural changes, effort, fatigue, or emotional upsets, or they may appear without relation to any such factors. They are characteristically variable from patient to patient with respect to severity, character of pain, and localization. This variability is characteristic of all groups of post-traumatic headache.

4. Headaches lasting for longer than two months were characteristically associated with dizziness and nervous symptoms (fears, anxiety, fatigue, irritability and/or inability to concentrate). This association is a statistical reflection of the composition of the well known post-traumatic syndrome.

5. The incidence of such prolonged headaches was high among patients with nervous or neurotic symptoms prior to injury, with complicating environmental factors (including compensation), with symptoms of marked immediate emotional reaction to the injury, and with scalp lacerations; it was low among recreational accidents, and among patients with very mild head injuries (no measurable duration of coma, disorientation, or permanent post-traumatic amnesia).

6. These relationships suggest the importance of both psychological and physical factors in the production of prolonged post-traumatic headache in the majority of cases. Even in headache localized to the region of known damage to scalp or skull psychological factors had high correlation.

7. A striking liability of headache localized to the site of previous scalp injury to provocation by posture or physical effort provides evidence that such provocation in more diffuse types of headache indicates underlying structural damage. A liability of provocation by histamine, particularly when the headache had been unilateral, suggests that intracranial localized vascular or perivascular change may occur.

8. Neither changes in the spinal fluid, in the electroencephalogram, in the reflexes, in the degree or extent of scalp or cranial injury, nor in the extent of disorder of consciousness immediately after the injury give adequate prognosis of subsequent liability to headache. Headache was, however, significantly less common in those who had no initial disorder of consciousness. Five of the 7 cases with no initial disorder of consciousness but persistent headache thereafter had localized scalp injury.

REFERENCES

1. Bremer, F., Coppez, H., Hicquet, G., and Martin, P. Le syndrome commotionnel tardif dans les traumatismes fermés du crâne. *Rev. Oto-Neuro-Ophtal.*, 1932, *10:* 161–224.

2. Denny-Brown, D. The sequelae of war head injuries. *New Engl. J. Med.*, 1942, *227:* 771–780; 813–821.
3. Friedman, A. P., and Brenner, C. Post-traumatic and histamine headache. *Arch. Neurol. Psychiat., Chicago*, 1944, *52:* 126–130.
4. Guttmann, E. Postcontusional headache. *Lancet*, 1943, *1:* 10–12.
5. Knoflach, J. G., and Scholl, R. Klinik und Prognose der stumpfen Schädelverletzungen. *Arch. klin. Chir.*, 1937, *190:* 452–522.
6. Lewis, A. Discussion on differential diagnosis and treatment of post-contusional states. *Proc. R. Soc. Med.*, 1942, *35:* 607–614.
7. Northfield, D. W. C. Some observations on headache. *Brain*, 1938, *61:* 133–162.
8. Penfield, W., and Norcross, N. C. Subdural traction and posttraumatic headache. Study of pathology and therapeusis. *Arch. Neurol. Psychiat., Chicago*, 1936, *36:* 75–95.
9. Pickering, G. W., and Hess, W. Observations on the mechanism of headache produced by histamine. *Clin. Sci.*, 1933, *1:* 77–101.
10. Rowbotham, G. F. Complications and sequels of injuries to the head. *Med. Pr.*, 1941, *205:* 379–384.
11. Russell, W. R. Cerebral involvement in head injury. A study based on the examination of two hundred cases. *Brain*, 1932, *55:* 549–603.
12. Schaller, W. F. After-effects of head injury. The post-traumatic concussion state (concussion, traumatic encephalopathy) and the post-traumatic psychoneurotic state (psychoneurosis, hysteria): a study in differential diagnosis. *J. Amer. med. Ass.*, 1939, *113:* 1779–1784.
13. Symonds, C. P. Discussion on differential diagnosis and treatment of post-contusional states. *Proc. R. Soc. Med.*, 1942, *35:* 601–607.
14. Woltman, H. W. Late neurologic complications of injury to the nervous system. *Wis. med. J.*, 1942, *41:* 385–391.

A METHOD OF HOLDING GALEA HEMOSTATS IN CRANIOTOMIES

F. ADRIAN KANTROWITZ, M.D.
Department of Neurosurgery, The Jewish Hospital of Brooklyn, Brooklyn, New York

(Received for publication July 27, 1944)

As one of the early steps in the standard technique of performing craniotomies for intracranial surgery, a number of small clamps are placed on the galea about one centimeter apart in order to secure hemostasis. Usually the hemostats are grouped together either by the use of a piece of gauze, or by winding a rubber band around them. A clamp was

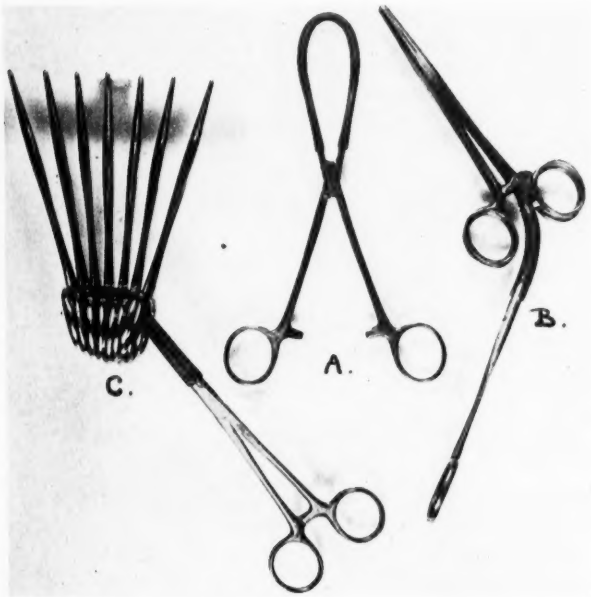


Fig. 1. *A*, Holding clamp showing rubber tubing attached to the blades; clamp open. *B*, Holding clamp applied to a single hemostat to show the application on one ring. *C*, Holding clamp applied to a series of hemostats showing its appearance and method of use in an actual operation.

devised in order to obviate the necessity of using these methods which at times are unwieldy.

A piece of latex rubber tubing about 0.5 centimeters in diameter and 14 centimeters long is drawn over the full length of the blades of an ordinary Carmalt clamp, as shown in Fig. 1. It was found that five or six hemostats can be held conveniently by one clamp. This method has the added advantage of holding the hemostats out of the way by applying additional weight. The application and removal of the clamp is simple, rapid, and dependable, if the blades are entirely covered by the ends of the rubber tubing.

The clamp has been used by the Department of Neurosurgery of The Jewish Hospital of Brooklyn and found to be convenient.

MECHANISM OF HEAD INJURY AS STUDIED BY THE CATHODE RAY OSCILLOSCOPE* PRELIMINARY REPORT

E. S. GURDJIAN, M.D., AND H. R. LISSNER, B.S., M.S.

Department of Surgery, College of Medicine and the College of Engineering, Wayne University, Detroit, Michigan

(Received for publication July 28, 1944)

CERTAIN aspects of head injury are well suited for study with the aid of the cathode ray oscilloscope. This instrument is particularly useful in connection with measurements of deformation of the skull and intracranial pressure changes that occur at the time of injury, since the element of inertia in the measuring and recording of the phenomena is entirely absent. A preliminary report of our investigations is given in this paper.

PROCEDURE

Mongrel dogs weighing 5 to 15 kilo were used in these experiments. Under intravenous nembutal anesthesia, the scalp was incised in the midline and the masseter muscles reflected and excised. After all bleeding points had been stopped, a small area of the skull was carefully dried and polished in preparation for the application of an electric strain gage. The strain gage was cemented to the polished surface of the skull with methyl methacrylate cement and this was allowed to dry under a heat lamp for approximately two hours. The strain gages used in these experiments were Baldwin Southwark SR-4 resistance wire gages, type C-5, having a half-inch gage length and a resistance of 350 ohms.

Two small holes were made in the temporal region of the skull with a number 25 drill and threaded with a number 10-24 tap. "Pressure plugs," which are made of a plastic such as celluloid or lucite about $\frac{1}{8}$ inch in diameter and $\frac{1}{2}$ inch long, are screwed into the holes. Two platinum wire electrodes run through each plug lengthwise, and the dura is opened so that they make contact with cerebrospinal fluid and the brain.

Fig. 1 shows an experimental preparation in which a strain gage was cemented longitudinally in the left parietal region and a "pressure plug" was inserted in the temporal region on each side of the skull. By means of an electronic switch operating at a frequency of 1,000 cycles per second, pressure readings from both sides of the skull were obtained simultaneously.

The use of the strain gage is quite common in industry for the study of deformations and stresses due to both static and dynamic loads.[1,2] It consists of a length of resistance wire 1/1,000 inch in diameter, cemented to a thin layer of paper. When the gage is cemented to the skull, the wire deforms as the skull deforms. When the skull bends inward, causing compression on the outside surface, there is a shortening of the strain gage wire with a consequent decrease in its electrical resistance. When the skull bends outward, producing tension on the outer surface, the wire lengthens causing an increase in its resistance. The changes in resistance are directly proportional to the changes in length which take place in the gages, and the resistance changes are recorded by the cathode ray oscilloscope.

Changes in intracranial pressure are recorded by the use of the "pressure plug," utilizing the fact that compression of an electrolyte decreases its electrical resistance and rarefaction or decrease in pressure causes an increase in its resistance.[3,4] With increase in intracranial pressure in the neighborhood of the "pressure plug," the electrical resistance of the cerebrospinal fluid between the platinum electrodes decreases, and the change of electrical resistance

* Aided by a grant from the Theodore A. McGraw Fund.

is observed on the oscilloscope. If the pressure is reduced this is also indicated by the increased resistance across the electrodes of the "pressure plug."

The electrical resistance changes occurring in the strain gage are measured by the potentiometer circuit shown in Fig. 2. G represents the 350-ohm strain gage which is cemented to the skull, R is a ballast resistance of 500 ohms, B is a 22½-volt battery, and S is a DuMont #208 cathode ray oscilloscope. Full gain of the amplifier in the oscilloscope was used with the strain gage experiments, giving an amplification ratio of the resistance change in the gage of 2,000 to 1. During the experiment, care had to be taken to prevent blood or moisture from coming in contact with the gage, and the wires of the circuit had to be attached to the gage in such a manner that no force or pull was exerted on the gage by the wires when the skull was struck.

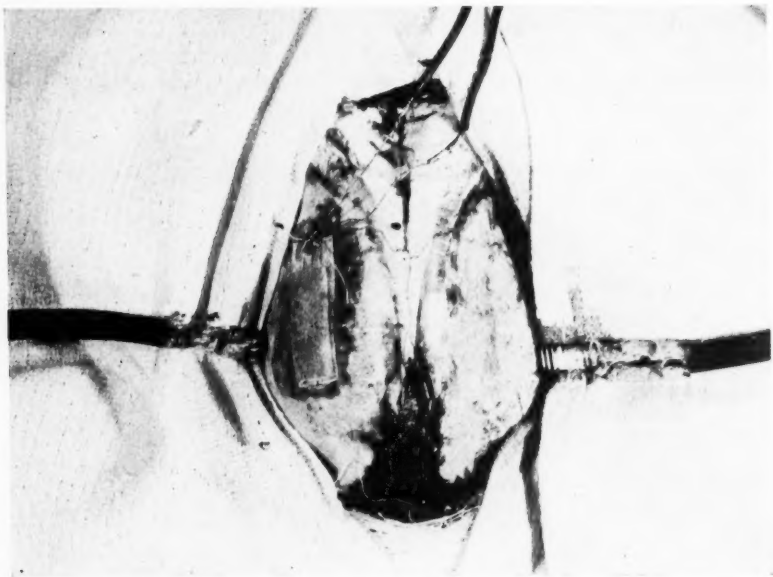


FIG. 1. Preparation with "pressure plugs" screwed into the skull and electric strain gage cemented to the left parietal region.

All connections were soldered to insure perfect contacts. In recording the picture on the screen of the oscilloscope, the horizontal sweep circuit was turned off so that the point of light moved only in a vertical direction. A camera having no shutter, in which the film moved horizontally past the oscilloscope screen at a rate of 17 inches per second was used for recording. A 60-cycle current of known voltage was also recorded by the camera for calibration of both the time and the strain functions.*

Fig. 2 will also serve to illustrate the circuit used for observing pressure changes. In this case G becomes the "pressure plug," the ballast resistance R is 25,000 ohms, B remains the 22½-volt battery, and S is the oscilloscope. The gain in the amplifier required in this case was much less than the 2,000 to 1 ratio used for the strain gage tests. Recording was done in the same manner as previously described.

* We wish to thank Messrs. F. G. DaRoza of the Fisher Body Corporation and C. Lipson of the Chrysler Corporation for the loan of some of the apparatus.

For the simultaneous recording of pressures from two plugs on opposite sides of the skull, each of two circuits, as shown in the diagram, are connected to the electronic switch, which in turn is connected to the oscilloscope. Since the time scale is the same for both pressure records obtained with the use of the electronic switch, one can observe the pressure conditions at two points within the skull simultaneously. The pressure records obtained by the use of the electronic switch in our experiments appear to differ from those obtained when recording only one pressure. This is due to the fact that the 1,000-cycle frequency of the switch was too near the frequency of the pressure waves being measured, and much better results would have been obtained had the switch had a frequency of about 10,000 cycles per second. However, our results do show definitely the trends of the pressures due to blows at various locations.

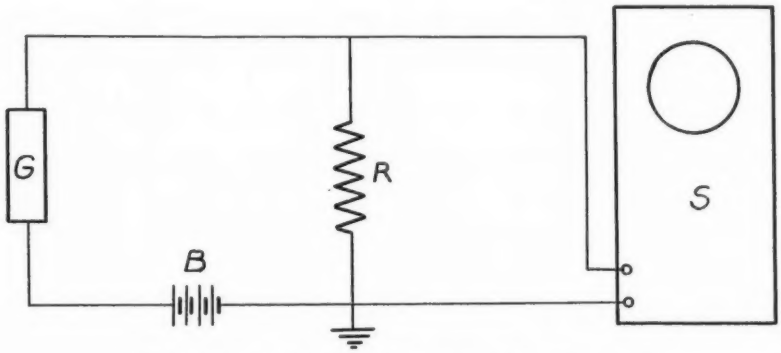


FIG. 2. Diagram of strain gage and "pressure plug" connections.

Accurate quantitative pressure measurements have not been obtained to date due to difficulties which are caused by the use of direct current across the electrodes of the "pressure plugs." It is hoped that these difficulties will be eliminated in future experiments by the use of alternating current instead of direct current or by a combination of direct and alternating currents.

EXPERIMENTAL DATA

Deformation of the Skull. When a hammer blow is administered to a skull that is free to move, the strain gage records indicate the nature of the deformation that occurs. When the blow falls on the same side with, and close to the strain gage, compression is indicated which is due to inbending of the skull. When the strain gage is on the opposite side from the blow, a tension occurs which indicates that the material is bending out or the radius of curvature is decreasing (Figs. 3A and B). The time necessary for the maximum deformation of the skull in the animals tested was approximately 1/2,000 second. Following the initial deformation the skull returns to its original shape and then two to four additional oscillations of deformation take place, the skull coming to equilibrium again in a time period of about 1/200 second from the start of the blow. With blows of varying intensity the magnitudes of the deformations change but the time periods of the initial deformations are essentially the same for all blows (Fig. 3C). That is, the time of initial

deformation of the skull is independent of the intensity of the blow, being about 1/2,000 second for each case in the animals tested. This time period will, however, be dependent on the size and shape of the skull.

Intracranial Pressures. Following a hammer blow to the same side of the skull as the "pressure plug" there is an initial increase in pressure in the re-

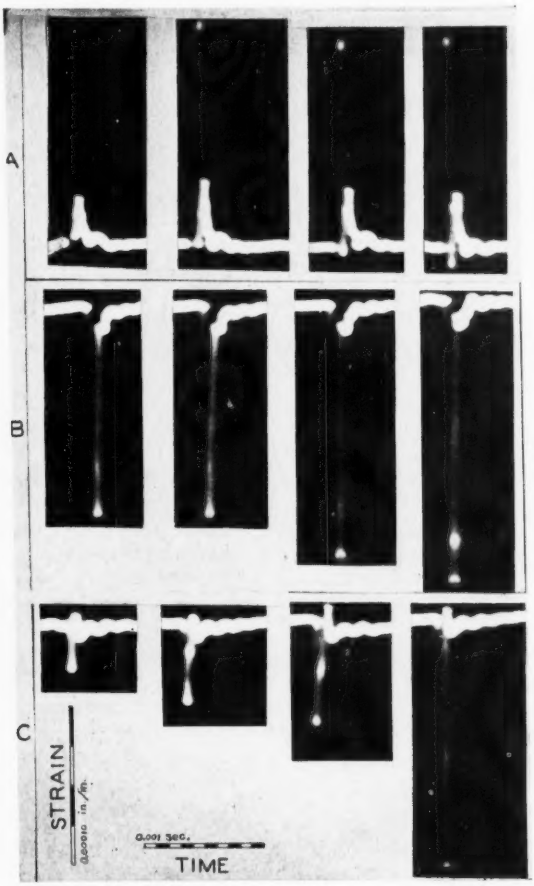


FIG. 3. Electric strain gage records of skull deformation. (A) Deformations in compression, (B) deformations in tension, (C) illustrates the fact that increasing the severity of the blow increased the amplitude but not the time of the deformation. The initial vertical sweep of the upper line of records has been retouched.

gion of the plug followed by two to four pressure oscillations before a state of equilibrium is again reached. Simultaneously at the side of the skull opposite the blow there is an initial decrease in pressure in the region of the plug (Figs.

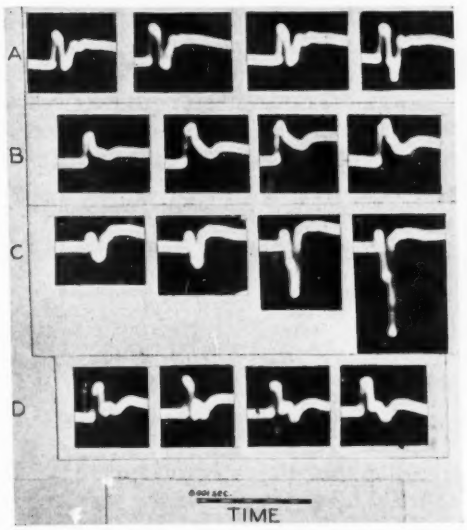


FIG. 4. Single line pressure readings with the "pressure plug" in the right temporal region. (A) Hammer blow in right occipital, (B) blow in interparietal, (C) blow in left occipital, and (D) blow in the interfrontal region.

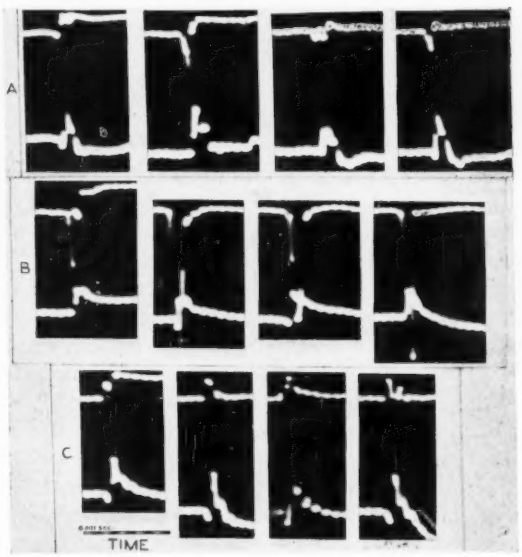


FIG. 5. Simultaneous recordings of pressure changes from both sides of the skull with the use of an electronic switch. "Pressure plugs" in right and left temporal regions. (A) Right parietal hammer blow, (B) left occipital hammer blow, and (C) interparietal hammer blows. In A and B diphasic records are obtained.

4A and C). The total duration of intracranial pressure oscillation corresponds very closely to that of the deformation of the skull. The time required to reach initial pressure peaks averages about 1/1,400 second for these tests. It is to be noted that this time is different from the time required for maximum deformation. The reason for the difference is that the skull usually does not reach its maximum acceleration until after the maximum deformation occurs and the greatest pressure will occur at the point of maximum acceleration. Since the pressure and deformation waves are not in phase they act to dampen each other and so bring both pressure and deformation to equilibrium in a short period of time. In Fig. 5, simultaneous pressure recordings from both sides of the skull demonstrate an increase in pressure on the side of the blow with decrease in pressure on the opposite side (A and B). When the blow is applied to the interparietal region there is an increase in pressure on both sides at the same time.

CONCLUSIONS

At the time of a hammer blow there is compression deformation of the outer surface of the skull at the site of the blow, and simultaneously at the side opposite there is tensile deformation on the outer surface of the skull or a bending outward. Simultaneously with deformation of the skull there is an increase in intracranial pressure on the side of the blow and a decreased pressure at the opposite side. The oscillations of deformation last about 1/200 second. The duration of pressure oscillations is also about the same. The frequency of the oscillations of deformation is about 700 cycles per second. The time required to obtain maximum deformation of the skull is about 1/2,000 second, and the time required to reach maximum initial pressure increase or decrease averages 1/1,400 second. These figures disagree with previously published reports of Scott,[5] who used the Hamilton manometer and concluded that the increase of intracranial pressure at the time of the blow lasted 4/10 second. In Walker's data,[6] however, the initial wave recorded by the Hamilton manometer corresponds closely to the total period of pressure change (1/200 second) recorded by the oscilloscope. It may be that the oscillations following the initial wave in the Hamilton manometer records are a function of the recording apparatus.

The existence of pressure waves in the cranial cavity has been demonstrated herewith. They may be a possible source of damage to the brain. This damage may be mechanical, with tissue injury due to dynamic stresses set up in the brain by the pressure gradient produced.

In conclusion it may be said that traumatic intracranial damage is due to deformation of the skull and changes in intracranial pressure brought about by deformation of the skull and acceleration of the head, after the blow.

SUMMARY

1. Deformation of the skull due to head injury has been recorded with the cathode ray oscilloscope.

2. A new technique for recording changes in intracranial pressure has been described.

3. At least two factors contribute to head injury through (1) deformation of skull, and (2) increased intracranial pressure setting up dynamic stresses produced by pressure gradients.

REFERENCES

1. De Forest, A. V. Characteristics and aircraft applications of wire resistance strain gages. *Instruments*, 1942, *15:* 112–114; 136–137.
2. Dohrenwend, C. O., Drucker, D. C., and Moore, P. Transverse impact transients. *Proc. Soc. exp. Stress Analysis*, 1943, *1:* 1–10.
3. Fanjung, I.* Über den Einfluss des Druckes auf die Leitfähigkeit von Elektrolyten. *Z. phys. Chem.*, 1894, *14:* 673–700.
4. Körber, F.* Über den Einfluss des Druckes auf das elektrolytische Leitvermögen von Lösungen. *Z. phys. Chem.*, 1909, *67:* 212–248.
5. Scott, W. W. Physiology of concussion. *Arch. Neurol. Psychiat., Chicago*, 1940, *43:* 270–283.
6. Walker, A. E., Kollros, J. J., and Case, T. J. The physiological basis of concussion. *J. Neurosurg.*, 1944, *1:* 103–116.

---

* Cited by Creighton, H. J., and Koehler, W. A. Principles and applications of electrochemistry. *New York: John Wiley & Sons, Inc.*, 1935, 3rd ed., *1:* 305–306.

THE TECHNOLOGY OF NERVE REGENERATION: A REVIEW. SUTURELESS TUBULATION AND RELATED METHODS OF NERVE REPAIR*

PAUL WEISS, Ph.D.

Department of Zoology, The University of Chicago, Chicago, Illinois

(Received for publication August 2, 1944)

INTRODUCTION

IN SEVERAL recent publications,[183,186,188,189,195,200] a method of sutureless reunion of severed nerve stumps by means of cuffs of artery was described and, on the basis of its merits in the laboratory, was recommended for possible adaptation to clinical use. The conclusions were based on experiments with a total of over 700 nerve unions effected in rats, rabbits, chickens, cats and monkeys, followed in the majority of cases by functional and histological studies. These experiments, in conjunction with a broader study of the mechanism of nerve regeneration, have led to important insight into the prerequisites for optimum nerve restoration. Arterial sleeve splicing complies with more of these prerequisites than do other methods, and this has been the basis of its success. But further application of the lessons thus learned gives promise of even more substantial improvements, and sleeve splicing may eventually be superseded by some other, more meritorious procedure incorporating its experiences. The emphasis lies more on the principle than on the current form of its application. An unbiased survey of existing methods of nerve repair, including sutureless sleeve splicing, shows plainly that no one of them is sufficiently superior to the others to deserve a monopoly of attention. In times of urgency such as these, the weighing of one method against another had therefore better give way to a concerted effort to extract the best features from all available methods and combine them to the best practical advantage.

Sleeve splicing bears a certain, though only superficial, resemblance to earlier procedures of joining the stumps of a severed nerve inside a tube ("tubulization") and of wrapping suture lines, procedures which have been practised on and off for more than sixty years (see Table 1). It also shares certain features with the method of plasma suture.[207,163]

None of the reported methods has been generally adopted, and there has been some controversy regarding their merits or demerits; many, in fact, have been thoroughly discredited.[155,130] Nevertheless, trust in their potential usefulness keeps manifesting itself in persistently recurring attempts to reintroduce them into the practice of nerve repair in either the old or some new form.[172,152] The very persistency of these attempts, aside from those simple

* Some of the experimental work referred to in this article was carried out under contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Chicago; also aided by the Dr. Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago.

TABLE 1

Main publications on nerve sheathing and tubulation

No.	Author	Year	Material Used
1	Gluck[58]	1880	decalcified bone
2	Vanlair[170]	1882	decalcified bone
3	Kölliker[98]	1890	decalcified bone
4	v. Büngner[23]	1891	artery; vein
5	Huber[85]	1895	Cargile membrane
6	Payr[124]	1900	magnesium
7	Pomerancew[131]	1900	decalcified bone
8	Lotheissen[106]	1901	gelatine
9	Foramitti[51]	1904	artery; live or fixed
10	Craig & Ellis[34]	1905	Cargile membrane
11	Sherren[142]	1906	Cargile membrane
12	Treutlein[169]	1906	artery
13	v. Auffenberg[7]	1907	decalcified bone
14	Hashimoto & Tokuoka[75]	1907	preserved arteries
15	Tilmanns[168]	1907	
16	Wrede[204]	1909	vein
17	Röpke[135]	1910	
18	Perekropoff[125]	1913	artery, vein
19	Denk[37]	1914	fascia
20	Eden & Rehn[44]	1914	fat tissue
21	Hirschel[79]	1915	preserved arteries
22	Auerbach[5]	1915	galalith
23	Fullerton[57]	1915	vein
24	Hans[70]	1915	epineurium
25	Heile & Hezel[76]	1915	unvulcanized rubber
26	Kirk & Lewis[95]	1915	fascia
27	Kredel[100]	1915	fascia and fat
28	Nageotte[117]	1915	vein
29	Bethe[16]	1916	artery
30	Edinger[45]	1916	agar tube
31	Mauclaire[110]	1916	trachea
32	Meisel[111]	1916	fascia
33	Auerbach[6]	1916	casein preparation
34	Stracker[157]	1916	veins; agar tube
35	Blencke[19]	1917	agar tube; artery
36	Burk[24]	1917	agar tube
37	Dustin[41]	1917	artery;vein; fascia
38	Eden[43]	1917	artery *in situ*
39	v. Enderlen & Lobenhoffer[47]	1917	artery; feather quill; agar tube
40	Hohmann & Spielmeyer[81]	1917	agar tube; artery
41	Kirschner[97]	1917	agar tube; fascia and fat
42	Müller & Berblinger[115]	1917	agar tube; artery
43	Perthes[126]	1917	fat tissue
44	Spitzy[151]	1917	agar tube
45	Steinthal[154]	1917	rubber
46	Bielschowsky & Unger[17]	1918	preserved dura
47	Meuriot & Platon[112]	1918	rubber
48	Platt[129]	1919	greased fascia; vein
49	Huber[87]	1920	artery, fascia, Cargile membrane
50	Stopford[156]	1920	fascia; vein
51	Kraus & Reisner[99]	1940	muscle, fat
52	Verne & Iselin[172]	1941	parchment
53	Spurling[152]	1943	tantalum

duplications of effort based on unfamiliarity with facts and literature, signifies that the belief in tubulating or wrapping suture lines stems either from a basic truth or a common delusion. The lack of unanimity in the matter can be ascribed to several reasons. One reason has been the fragmentary state of knowledge about nerve regeneration. Ignorance of the requirements of the different tissue components in nerve regeneration has turned some basically sound procedures into failures merely because some trivial fact, the importance of which had not been known or suspected, was neglected. Another difficulty has been the lack of objective and uniform standards in assessing and describing the experimental and clinical results. Moreover, there were many reports without adequate documentation and many claims unsupported by facts.

This state of affairs has made it desirable to reexamine the whole subject in the light of the increased knowledge and more critical standards of today. The following report undertakes to do this in the spirit of scientific analysis. Neither the biological process of nerve regeneration nor the various techniques to facilitate it for the sake of functional nerve restoration are indivisible wholes. All components of a nerve and of its surroundings—axons, sheath cells, fibroblasts, macrophages, erythrocytes, leucocytes, plasma, collagen, capillaries, etc.—all these contribute in some degree to the outcome of nerve regeneration, and their various peculiarities and requirements want to be taken into account. Every technique of nerve union, in turn, consists of a variety of steps and measures each of which is apt to affect differentially the various tissue components, some beneficially, and some adversely. The net balance decides the outcome for nerve regeneration as a whole, whether beneficial, harmful or irrelevant. There is no justification, therefore, for either accepting or condemning any one method *in toto*, since each one must contain elements worth preserving and exploiting, as well as elements patently detrimental, and elements that do neither good nor harm. By sorting out these elements, scientific analysis prepares the synthesis of improved methods, which will emerge from the combining of the positive features of the different techniques and the elimination of their recognized drawbacks. The results, subject to verification in laboratory experiments, may then be adopted as blueprints for clinical procedures.

THE MECHANISM OF NERVE REGENERATION

Due regard for the realities of nerve regeneration is essential both in judging existing methods of nerve repair and in devising new procedures. Any methodical approach to the problems of nerve repair must be based on strict observance of the growth requirements of regenerating fibers, which in turn presupposes intimate knowledge of nerve growth, and this means not merely descriptive knowledge of the phenomena as recorded in macroscopic and microscopic observation, but analytical understanding of their mechanics. Some valuable progress in this direction has been made during recent years, even though it is still small in the light of what remains to be done. As a di-

rective for future research, it must be stressed that progress in this field is not to be expected simply from continued search for more facts along the classical lines of nerve regeneration studies, but from a basic change of viewpoint. Problems of nerve regeneration will have to be taken out of the province of naturalistic description and transferred into that of physical and chemical reality, where nerves are treated as material systems with verifiable physical and chemical properties. A similar reorientation is noticeable in all current biological thinking, and the field of pathology has greatly benefited from it. Morphological features formerly described as such must be resolved into the dynamics operative in their formation.[182,122] In the case of the nerve fiber, the mere listing of such phenomena as local swellings, terminal bulbs, spiraling, branching, etc., must give way to a dynamic concept of the mechanism of nerve growth so consistent that all those phenomena will appear as logical manifestations of that growth principle under the locally prevailing conditions.

There have been some good efforts to that end in the past, but most of them were either very abstract or based on inconclusive experimentation. The very phenomenon of "growth" of the nerve fiber has only occasionally been stated in sufficiently articulate form to invite analysis.[185,205] If "growth" connotes augmentation by synthesis of the living substance, how much of the elongation of a regenerating axon is due to real growth, and how much to mere draining of preexisting substance from the cell body? And does what actual growth there is occur in the cell body, at the advancing tip, or over the whole length of the axon? And where are the ingredients for this synthesis taken in—centrally, at the tip, in the whole naked part, or at the nodes of the old stump? And does what is valid for the elongation of the fiber hold equally true for its continued growth in width? It is tangible questions like these that will have to guide research, rather than just general talk about "growth" in all its indefiniteness. What sense is there, for instance, in speculating on how essential are blood supply, vitamins, etc., to the young fiber sprouts if one does not even know to what extent the latter depend on local sources for their oxygen and nutrient supply?

Another example of the lack of concern for physical realities which characterizes much of the past work on nerve regeneration is the not uncommon tendency to view nerve fibers, at one time, as if they were growing in a vacuum, and at other times, as if they were not corporeal. One encounters descriptions (occasionally in connection with tubulization experiments) according to which the space into which nerve fibers grow is "empty."[19,43,151,157] Now, physically speaking, there can be no empty space anywhere in an organism; there must be either solids, liquids, gases, or mixtures of them, and the behavior of the nerve fiber will vary significantly, depending on how the space is occupied. The fallacy of identifying lack of histological distinctiveness with physical homogeneity is obvious. On other occasions, the ability or inability of nerve fibers to "grow through" other tissues is discussed with insufficient regard for the physical mass of the fiber. This is very pertinent to

such problems as the penetration of scars, invasion of grafts, etc. Obviously, a nerve fiber, like any other physical body, can penetrate another tissue only by displacing a corresponding volume of substance, and since only liquids are freely displaceable, the penetration of nerve fibers, as well as their continued growth and expansion, will be limited by the liquid content of the tissue and possible liquefying potency of the fiber (see below).

These examples may suffice to indicate the need of greater concreteness in dealing with the problems of nerve growth. The following outline of the mechanics of nerve regeneration is a step in this direction. Only those aspects of the larger problem will be taken up that are of immediate bearing on problems of nerve suture. A basic familiarity of the reader with the descriptive facts of nerve regeneration will be taken for granted.* To avoid misunderstandings and for easier reference, the sense in which various terms will be used in this article is defined in the following list.

TERMINOLOGY

Proximal Stump. That part of a severed nerve left connected with the centers.

Distal Stump. That part of a severed nerve disconnected from its centers.

Aneuritic[109] *Nerve.* Nerve after degeneration of all axons.

Gap. The space between the cut faces of two nerve stumps.

Union Tissue. The tissue filling the gap and interweaving the formerly separated stumps.

Matrix. The non-cellular foundation of the union tissue.

Scar. Union tissue with excessive fibrous development.

Junction. The level at which the nerve stumps are reconnected, which after suture is the "suture line," but after sutureless splicing includes the whole extent of the union tissue.

Schwann Cells. The accessory sheath cells of the nerve fibers, both in their normal tubular state and after the hyperplasia attending Wallerian degeneration.

Neurotization.[171] Invasion of a tissue by nerve fibers, e.g., the repopulation of a distal stump by regenerating branches, or the reinnervation of denervated skin and muscle.

Neurilemmal Tubes. The fibrous tubular surface covering of the individual nerve fiber, variously identified as sheath of Henle, Key-Retzius, and Plenk-Laidlaw; regardless of its origin from, and relation to sheath cells, endoneurial cells, or both (see Young[205]); for brevity, called "tubes."

Endoneurium. The connective tissue occupying the spaces between the individual nerve fibers.

Macrophages. Solitary phagocytic cells of hematogenic or histiogenic origin giving the appearance of common macrophages.

Neuroma. An irregular excessive growth containing a dense tangle of nerve fibers.

Glioma.[119,41,109] An irregular excessive growth from an aneuritic nerve, composed largely of Schwann cells.

Edema.[187] Distension of the endoneurial spaces by excess fluid.

NERVE DEGENERATION

A nerve is a composite structure. Its constituent elements—axis cylinders, Schwann cells, tubes, endoneurium, perineurium, epineurium, blood vessels—react differentially to the trauma of transection, their combined responses in the distal stump forming the syndrome known as Wallerian de-

* For reviews of the descriptive histology of nerve regeneration, the reader is referred to the works of Ramon y Cajal,[31] Ranson,[133] Huber,[88] Nageotte,[119] Boeke,[21] Rossi and Gastaldi.[137]

generation.[31,119] Degeneration precedes and, in a sense, prepares the ground for regeneration. It involves regressive and progressive changes. Most prominent among the regressive changes of the distal stump is the breakdown of the myelin sheath and the axis cylinder, followed by the dissolution and resorption of the resulting debris (with formation of so-called digestive chambers or "ovoids"). Progressive changes include the appearance of large numbers of macrophages removing nerve debris, and the conversion and proliferation of formerly tubular Schwann cells into solid cell strands (Büngner's cords). In addition, common traumatic and inflammatory reactions may occur at the wound surfaces. In the proximal stump, degenerative changes similar to those of the peripheral stump remain confined to the vicinity of the wound, their extent varying with the nature of the trauma from a few millimeters to several centimeters. They are soon to be superseded by the regenerative processes in which the proximal stump takes the lead.

Save for a few resistant fibers, the regressive changes of the distal stump are nearly completed within a few days after transection. Whether or not degeneration proceeds in proximo-distal direction down the nerve, is still controversial.[23,83,159,123,84,136] The factors controlling Wallerian degeneration are, in spite of some analytical attempts,[119,90] still largely unknown. Its rate varies with the circumstances; it is markedly delayed by nerve compression.[194] Experiments to determine whether nerve fragments which have degenerated at different rates and under different conditions are all equally suitable for neurotization, are under way.

The neurilemmal tubes survive the lytic processes of early degeneration. They become distended by the accumulation of decomposition products and macrophages. This increase of turgor, causing swelling of the nerve as a whole (for actual measurements, see Weiss[187]) and obliteration of the endoneurial spaces, may interfere with blood circulation and stimulate collagen deposition,[109] but no further information on these points is available. Variations of turgor may be the clue to the later differences in fibrosity between different aneuritic stumps and, if so, would be of clinical importance.

Schwann cell reaction promptly follows the fragmentation of the axis cylinder. There are indications that the Schwann cells participate in the digestion and perhaps even phagocytosis of the tube content during the initial phase of degeneration.*[,31,119,41] In fact, direct intake of degeneration products might account for their rapid hypertrophy. However, the main share of the clearing of the tubes is soon taken over by the macrophages, which appear on the scene in large numbers.[118] Their exact origin has never been traced. Many are undoubtedly transformed blood monocytes. Mobilized histiocytes might enter through the wound surface if the latter were left exposed. However, since macrophages are just as numerous in sleeve-spliced nerves[200] (in which immigration from the surroundings is precluded), this source cannot be important. A third conceivable source lies in a possible

* In recent tissue culture studies (still unpublished), Schwann cells from peripheral nerve were actually observed in the act of digesting ingested myelin.

conversion of some Schwann cells and endoneurial cells of the nerve itself into macrophages. Although actually observed in tissue culture,[191] the occurrence of such a transformation in nerves *in situ* has not yet been demonstrated. The problem is of considerable practical importance since the ratio between Schwann cells and macrophages in the distal stump has a bearing on the subsequent neurotization process.[191]

The final fate of these macrophages is uncertain. From the standpoint of successful nerve degeneration, it would be desirable to have them move on after ingesting the debris of the tubes so as to make room for the cords of hypertrophied Schwann cells. As a rule, this occurs. However, under certain still undefined conditions, the macrophages remain trapped inside the old tubes, thus preventing the expansion of Schwann cells and barring the entry of regenerating nerve fibers. I have seen aneuritic tubes crammed with immobilized macrophages many months after transection,* and since this condition may well become a permanent obstacle to neurotization, further exploration of the origin, behavior and fate of macrophages as a basis for improved control over their activity in nerve regeneration is urgently needed.

Mitotic activity of the expanded Schwann cells sets in within a week[23] and the enlarging strands (a) fill the tubes,[21,82,119] except where "ovoids" and macrophages resist replacement; (b) appear in intertubal positions,[31] partly from former unmyelinated fibers, partly perhaps after escaping through "leaks" in tubes; and (c) spill from the open ends of the tubes into the surroundings, initiating what is often referred to as the "glioma,"[41,119] or "Schwannoma"[109] of the peripheral stump.

All these component processes of Wallerian degeneration are interdependent so that interference with any one of them may alter the course of all, which in turn may seriously affect the subsequent neurotization processes for which they are to prepare the proper setting.

Neurotization, i.e., the supply of new axis cylinders, definitely has been shown to be solely a function of the proximal stump. The concept of "autogenous" nerve regeneration,[14,150] has been conclusively disproved.[31,119] The role of the converted ("degenerated") distal stump is merely that it presents to the outgrowing axons conditions of growth far superior to those offered by any other known environment. This explains why the exploration of the properties of degenerated nerve must be carried on as an integral part of all research on nerve regeneration. First, the degenerated stump does not invariably attain that state of optimum receptiveness for regenerating fibers of which it is intrinsically capable, and knowledge of the reasons for this variability may suggest measures by which that optimal condition may be brought about more consistently; this is particularly evident in the case of nerve grafting in which the often reported inferiority of distal nerve fragments, when used as grafts, contrasts with their effective neurotization when left in place. Unsuspected differences in local conditions can account for such variety of results as that one distal nerve fragment becomes a superb

* Compare also figure in Hammond, Nonidez and Hinsey.[69]

bed for regenerating fibers, while another becomes a dense, almost impervious, fibrotic strand, and a third remains clogged up with macrophages. Second, insight into the biophysical and biochemical peculiarities to which degenerated nerve owes its superiority as a growth bed may make it possible to provide growing nerve fibers with their essential prerequisites even in the absence of degenerating nerve, so that perhaps in the future synthetic substitutes for nerve grafts may be devised from this knowledge.

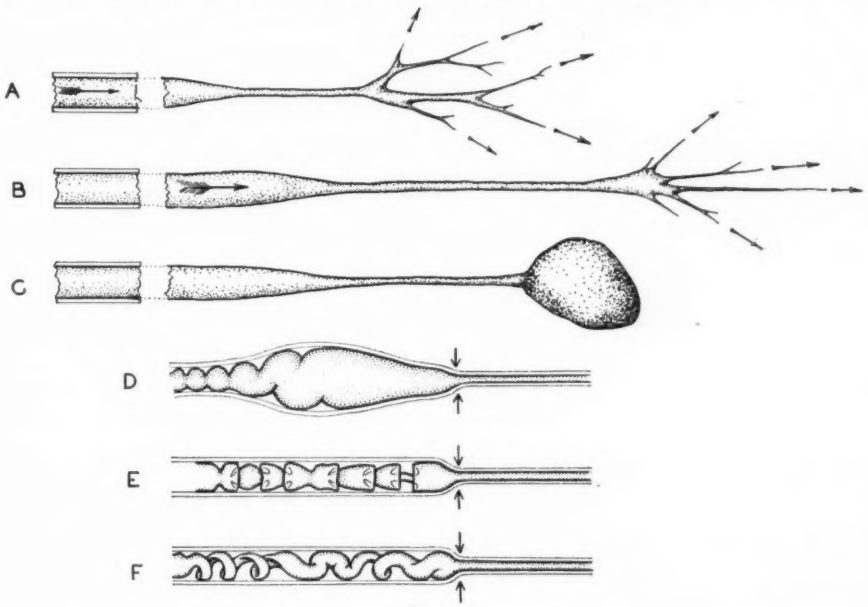


FIG. 1. Diagrams illustrating normal and impeded outgrowth of axons. *A*, *B*, Two successive stages of outgrowth showing progressive elongation by interfacial tensions (simple arrows), which draw out the transitory terminal filopodia to fine points, followed by lateral enlargement resulting from centrifugal convection of axonal substance by intraaxonal pressure (feathered arrow). *C*, Terminal bulb, produced by the damming up of axonal substance in front of an unsurmountable obstacle. *D*, *E*, *F*, Ballooning, telescoping, and coiling of the axonal substance just proximal to a constriction which reduces the diameter of the tubes (level of constriction indicated by arrows). Centrifugal growth pressure in the axon continues to move axonal substance distad, and the damming up of this substance in front of the "bottleneck" leads to the various forms of contortion shown in these schematic reproductions from photomicrographs.

NERVE REGENERATION

The outgrowth of new axons from the proximal stump is the cardinal process in nerve regeneration. As such it has monopolized much of the attention in the past, an attitude accentuated by the preferential use of silver impregnation methods, which visualize the axis cylinder practically to the exclusion of all other structures. It is well, however, to bear in mind that the distal nerve stump, into which the new sprouts grow, makes some substantial, even though less spectacular, contributions to their growth, and that the

full restoration of a nerve is a compound process involving the participation not only of the axis cylinders but also of those accessory elements of their surroundings on which they depend for nutriment, guidance, protection, myelinization, maintenance, and perhaps other as yet unrevealed influences. Consequently, nerve regeneration must never be dealt with in terms of the growing axon alone, but always in reference to the environmental conditions under which growth takes place.

The so-called outgrowth of the regenerating axon is primarily protoplasmic movement of the amoeboid type.[71,74,102,177] The tip of the axon becomes mobile and extends into the environment by means of fine filamentous pseudopodia ("filopodia").[114,143,144,145] As it proceeds, it spins out the axoplasm behind it to increasingly greater length (Fig. 1A, B). The motive force

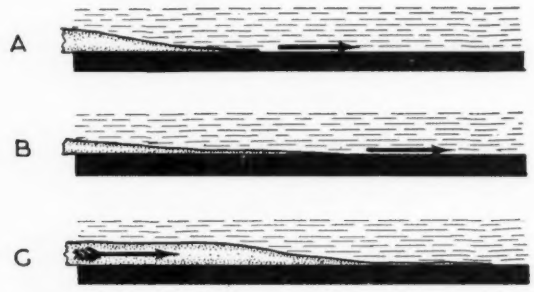


FIG. 2. Pull-push mechanism of nerve fiber advance. Drawn out by interfacial tensions (simple arrow) along solid-liquid interface, fiber receives inflow by intraaxonal pressure (feathered arrow).

actuating this elongation has often been ascribed to pressure inside the neuron (Held's[77] "vis a tergo"; Cajal's[31] "formative turgor"; Young's[205] "outflow"). Evidence of such pressure has been found in the familiar terminal bulbs of arrested nerve fibers (Fig. 1C),[31,41,205] and more recently in the swelling of locally compressed nerve fibers immediately proximal to the level of compression (Fig. 1D, E, F).[192,197] On physical grounds, however, such pressure cannot of itself account for the extension of the filopodia. It is necessary to assume some external pull, which is obviously exerted by interfacial tensions[185] (Fig. 2).

Nerve fibers can extend only along phase boundaries between two media and cannot move into a homogeneous medium in the manner of plant roots.[72, 177] They are drawn out along a solid-liquid interface (Fig. 2A, B) by forces roughly comparable to those causing oil to spread along a water-air interface. Flow of axoplasm into these pseudopodia, presumably sustained by intraaxonal pressure, then fills them up (Fig. 2C). The advance of the axon is thus due to a pull-push mechanism, with interfacial tensions exerting the pull, and internal pressure pushing from behind. Of the several filopodia appearing concurrently, usually only one receives the main inflow, while the

others are withdrawn.[144,145] Inflow divided over several filopodia gives rise to terminal branching.[144,185]

This pull-push advance of the fiber tip can proceed for some time *in vitro* in pure inorganic media containing no nutrients or growth implements, such as thiamin or biotin, other than those possibly stored in the nerve cell.[28] This observation suggests that early "outgrowth" is a physical process of elongation, rather than a true "growth" process involving chemical synthesis of new axoplasm. The same conclusion has been reached from the observation that the proximal diameter of nerve fibers decreases during the early stages of regeneration.[67] Only secondarily does the physical elongation then entail increased assimilation and thereby initiate actual growth for the consolidation of the fiber. After the fiber has reached its full length, it continues to grow in width. This growth has been shown to proceed from the central cell body.[202] In reality, the situation is even more complex than here outlined, but this brief sketch will suffice to indicate the intricacy of the mechanism of nerve fiber "growth," and, accordingly, the diversity of provisions required to support it.

The linear character of nerve growth raises the question of what factors orient the outgrowing fibers. Concretely, this problem resolves itself into two questions: what guides the advancing pseudopodia, and what determines which pseudopodia are to become consolidated and which are to be resorbed. Once the tip has been caused to move in a given direction, the rest of the fiber follows automatically. If the tip moves straight, the fiber course will be straight, while an erratic course of the tip will result in contorted fibers, though some bends may later be straightened out by elasticity. Answers to the problem of what guides the fiber tip have been proposed in essentially four different theories: (1) Contact guidance[40,74,80,177,185]; (2) Least resistance[171]; (3) Chemotropism ("neurotropism")[30,31,53,54,107,167]; (4) Galvanotropism.[26,32,93,158] These have been discussed more fully on previous occasions,[38,74,185] and only the most pertinent points will be repeated here.

Contact Guidance. "Contact guidance" implies that the growing tip applies itself blindly to the substratum with which it is in contact. The course of the tip is, therefore, determined solely by the configuration of its contact environment plus such physical and chemical properties of the latter as will make for adhesion or non-adhesion and intimacy of the resulting contact. The original concept, that nerve fibers follow gross mechanical structures,[73,80] is incomplete. It has to be extended to the submicroscopic field.[177] As stated before, fibers can grow only along surfaces; but it takes some additional factor to single out a particular direction along that surface to be followed. This directive factor is presumably provided by the fine structure of the surface. Extensive experimental evidence has been presented,[177,185] to show that nerve fibers follow the direction of oriented fibrillar units of microscopic or submicroscopic dimensions present in their contact substratum. Additional evidence will be cited below.

Both cellular and non-cellular surfaces may serve in the capacity of con-

tact substrata. But in either case, the line of advance is determined by some linear structures ("pathway structures") within that surface. Fibrin fibers are excellent climbing ropes,[177,200] and so are Schwann cells.[96,119,200,205] It is significant that oriented interfaces orient fibroblasts[176] and Schwann cells[177] just as they do nerve fibers. They can, therefore, orient nerve fiber growth either directly or through the intermediary of a correspondingly oriented spindle cell which the nerve fiber then follows. Moreover, nerve fibers already in existence form, under certain conditions, preferential pathways for other advancing nerve tips, which fact accounts for the building up of nerve bundles around pioneering fibers ("fasciculation").[185]

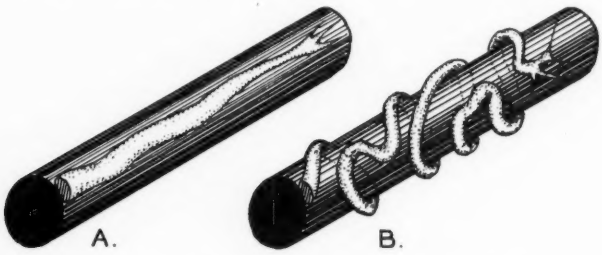


FIG. 3. Straight polarized advance of axons in the direction of the axis of a fiber serving as substratum (*A*); contrasted with the random winding course (*B*) to be expected if either simple "stereotropism" or "least resistance" were the determining factors. [A winding course is observed only (a) if the substratum has a spiral surface organization (e.g. in Perroncito's coils), or (b) if the fiber is arrested in its advance, yet keeps increasing in length (e.g., Fig. 1, *F*), or (c) if a fiber retracts.]

Contact guidance, as here described, implies that the nerve fiber tip reacts solely to cues of its immediate environment. Agents acting from a distance can, therefore, influence the course of a nerve fiber only to the extent to which they affect the physical pathway. Selective affinities between different types of nerve fibers and different kinds of pathways are a possibility worth keeping in mind,[166] although the evidence in favor of selective outgrowth is still incomplete.

Least Resistance. The theory that nerve fibers simply take the course of lowest mechanical resistance—one of the earliest concepts,[171] and one still sporadically encountered in current literature[69]—is partly incorrect and, for the rest, non-committal. Let us recall, for instance, that nerve fibers do not grow into homogeneous fluids, even though the mechanical resistance of liquids is negligible; also that nerve fibers, given an appropriate pathway structure, can grow from a softer into a denser medium,[177] unless the latter is impenetrable (see below). Moreover, "least resistance" cannot explain why fibers which extend along a solid-liquid interface follow definite directions, rather than just move about at random, as the all-round absence of obstacles would enable them to do. Axons on a fibrin thread in serum, for instance, follow a straight longitudinal course (Fig. 3A), and do not wind themselves

around the thread (Fig. 3B).* Thus, while it is unquestionably correct to state that nerve fibers are deflected by mechanical obstructions, it takes something more positive than mere lack of obstacles to define their actual course. What serious consequences superficial thinking in these matters may have when applied to practical problems, is well illustrated by the notorious Edinger tubes, introduced during the last war for the bridging of nerve gaps[45] (see below). These were tubes, filled with gelatin or agar-agar, interposed between the nerve stumps. The idea was to present the outgrowing nerve fibers with a "soft" medium. Yet, no fibers grew in—as we now realize, for lack of proper interfaces—and the method proved a sad failure.[81,151,157] Fiber growth needs positive support, not just absence of handicaps.

Chemotropism (neurotropism). The theory that growing nerve tips are attracted toward distant sources of chemical emanations by a mechanism of chemotaxis was first suggested by Cajal[30] and later specifically applied to nerve regeneration.[31,53,54,107,167] It endows the nerve tip with the capacity to perceive and discriminate different chemicals and to orient itself uphill along the concentration gradient leading to their source. Particularly strong attractive potency was ascribed to peripheral nerve in the state of degeneration. It seems that this theory is based wholly on the misinterpretation of experiments undertaken to prove it. Not only are those earlier experiments amenable to other than chemotactic interpretations,[40,91,185] but more recent experiments, carried out under more critically controlled conditions,[201] have conclusively disproved the existence of any chemical attraction or chemotactic orientation of regenerating nerve fibers by tissues in general, and degenerating nerve stumps in particular. Results formerly attributed to "neurotropism" can be ascribed to the orienting effects of tension exerted by the nerve stumps on the intervening union tissue serving as pathway for subsequent nerve growth, plus the accentuating effect produced by fiber aggregation[185] ("fasciculation").

This rejection of the theory of "neurotropism" applies only to the thesis of an attraction of nerve fibers towards distant destinations. That the adhesion of nerve fibers to their like, as well as the effectiveness of synaptic and peripheral connections, might be determined by chemical affinities operating after contact is established, is merely a special aspect of the contact guidance theory discussed above.

Galvanotaxis. The theory that fiber growth is oriented by electric fields,[26,32,93,158] is contradicted by the observation of nerve fibers growing simultaneously in opposite directions.[144,177] Moreover, all experimental tests of the theory have been consistently negative,[60,94,177,203] except for one supposedly positive experiment,[92] in which, to all appearances, mechanical effects were mistaken for electrical ones.[177]

* This statement is based on extensive studies on nerve growth along surfaces of different configurations in tissue culture. The results of these studies will be reported more fully on a later occasion.

Nerve Outgrowth. According to the foregoing survey, the tip of the regenerating axon is guided in its advance by structural characteristics of the substratum with which it is in contact. The growing axon traces patterns of its surroundings. Random patterns, such as are presented, for instance, by nerve scars, lead to correspondingly confused nerve growth. Conversely, orderliness of nerve growth presupposes the presence of well aligned parallel pathways. Degenerated nerve offers such pathways in abundance both along the inner and outer surfaces of the tubes and along the strands of Schwann cells. In the gap, however, beyond the limits of degenerated nerve, oriented nerve growth can be enforced only if we provide the nerve fibers with a new system of pathways of the proper constitution and proper orientation. The guiding role of Schwann cells is still controversial. According to some authors,[41,96,119,205] they precede the axons, laying down the tracks, as it were. According to others,[31,69] most axons sprout out independently. Observation under especially favorable conditions[200] has shown that, generally speaking, Schwann cells have a head start over the axons and that the axons, perhaps for this very reason, tend to cling to the Schwann cords. At the same time, examples of freely outgrowing axon tips were observed, even though relatively rarely. Obviously both forms of outgrowth occur, with axon orientation being effected, in one case through the mediation of Schwann cords, previously oriented by the pathway structure, in the other case by the pathway structure directly.

Parallel guide lines in the pathway structure are not only prerequisite for the orderly parallel outgrowth of Schwann cells and axons, but are also instrumental in keeping fibrous connective tissue from intruding into the path of the nerve. Fibroblasts align themselves along linear structures,[73,176] just as do Schwann cells and axons. Consequently, the same oriented structural pattern that guides the nerve fibers also deflects extraneous connective tissue cells and collagen fibers into a longitudinal course along the surface of the nerve, which is a useful course. For here the connective tissue is led to build a new sheath over the gap, instead of penetrating into the path of the nerve where it would scarify and impede regeneration. It may be impossible to prevent scar tissue from forming near a wound, but it is perfectly feasible to render it innocuous by directing it into a course parallel to the nerve where it can do no harm. A parallel pathway structure, therefore, both guides nerve growth and protects it against interference. How then can such favorable pathway structures be established?

Fibrillar structures consist of an oriented array of linear colloidal particles.[56,128] Under random conditions, such particles clump into a spongy framework. If aligned in parallel orientation by some external orienting force they join end-to-end and flank-to-flank, building up larger linear units. The formation of fibrin fibers, for instance, occurs in this manner.[9] The most potent and common force to produce such parallel alignment is mechanical tension.[9,42,176,177] Not only has its orienting effect on colloids long been

known, but its molding action on tissues has been amply demonstrated and experimentally tested. Rod-shaped ultramicrons become oriented and aggregate along the lines of prevailing tension. Parallel tensions, therefore, produce fibrils and fibers of corresponding parallel orientation (Fig. 4A).

Tensional stresses arise either from external stretch or from internal shrinkage. An example of stresses arising from shrinkage may be seen in the cracking of drying soil. Local condensation of fibrous tissue, the familiar scar contraction, is a common source of such internal stresses and is very perti-

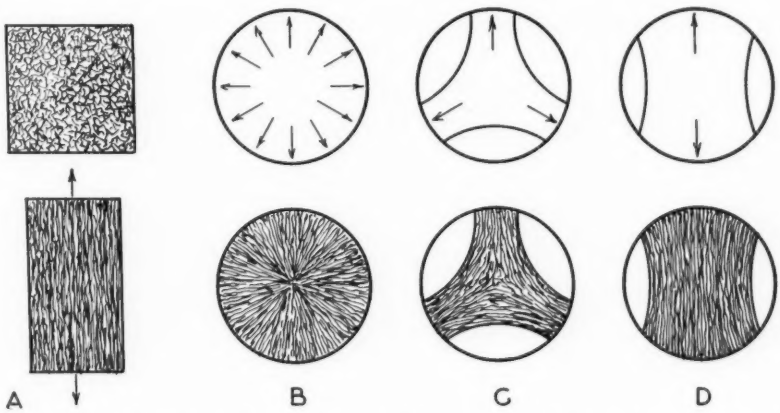


FIG. 4. Effects of tension on fibrous colloids. *A*, Colloid with anisodiametric elements in chaotic arrangement (top), when stretched, assumes orientation in the direction of the prevailing tension (arrows). *B*, *C*, *D*, Tension patterns (top row) and resulting fibrillar orientation (bottom row), arising from the shrinkage (e.g., syneresis) of a colloidal matrix firmly attached to its frame along the whole circumference (*B*), detached on three sides (*C*), and detached on two sides (*D*).

nent to problems of nerve suture. The stress pattern is not determined solely, however, by the tensions imposed on the tissue or generated within it, but also by the elastic and plastic properties of the different tissue components. Stress will develop only in those directions in which the tissue does not yield to the deforming force. And since the tissue will yield in all directions in which it is not prevented from yielding by firm attachments, the points of attachment of a tissue under tension are critical parameters of the resulting stress pattern (Fig. 4B, C, D).

In conclusion, a stress pattern lasting sufficiently long to impose its orientation upon the tissue matrix becomes thereby a primary factor in the laying down of pathways for nerve fibers and spindle cells. Conditions thus created affect not only the orientation of growth, but also its rate, as well as the density of the resulting new tissue. To have brought these problems down to earth, from the speculative language of "trophic stimuli" and "attractive influences" to the factual treatment in terms of technology and

physico-chemistry, has been an essential step toward rational understanding and control of the mechanics of nerve regeneration and tissue repair.

Advance of healthy nerve fibers and sheath cells can proceed as long as there is an unobstructed pathway; hence, failure to advance in the proper direction will have to be ascribed to either lack of pathways or diversion of existing pathways or inadequacy of the physical and chemical conditions along the pathway. Physical inadequacy results from excessive density of the tissue to be penetrated. In order to appreciate this point, one must visualize the actual physical setting in which nerve regeneration takes place. Axons and Schwann cells invade the tissue of the gap, and axons invade the distal stump. If the tissues to be invaded were solid and compact, invasion would be physically impossible because one physical body (nerve fiber) can move into the space occupied by another physical body (distal stump) only by replacement, that is, to the extent to which it can force out of place an equal volume of the latter. And since only liquids, or solids suspended in liquids, are freely displaceable, the capacity of any tissue for receiving new cells and nerve fibers will be limited by its content in liquids and the ease with which these can be shifted (capillarity, viscosity, etc.). The less liquid space a tissue contains, that is, the denser it is, the fewer fibers will be able to penetrate, and the slower also will be the advance of those which have entered; just as it takes more time to drive a nail into hardwood of dense texture than into softwood of spongy texture.

Under certain conditions, an invading tissue makes room for itself by liquefying (digesting) the invaded tissue as it goes along. Some proteolytic activity has occasionally been observed near nerve fibers growing *in vitro*[177,185] and signs of it can be seen around arrested growth cones.[41] But it is uncertain whether it normally occurs during regeneration and, even if it did, experience has shown that it would be impotent to proteolyze dense collagenous scar tissue. The possibility that the growing axon may absorb some substance directly from adjacent Schwann cells so that it could expand at their expense, cannot be excluded, but no definite information on this point is available.

Without proper room for continued expansion, nerve fibers, even though they may have reached the periphery, cannot swell from the small diameter (1μ or less)[13,31,67,82,133,134] at which they grow out, to the large dimensions of the mature fiber. Therefore, both in the interest of primary outgrowth and of later size increase, due consideration must be given to the space requirements of the new nerve fibers, and this is just as important as is emphasis on proper orientation of the pathway. Tendons have perfect orientation, but are far too dense to serve as conduits for nerve growth. The same is true of heterografts,[86,140,190] and alcohol- or formalin-fixed grafts[67,86,119,139] of nerve or muscle, inasmuch as these are progressively transformed into tough fibrous connective-tissue strands, assuming a texture not unlike that of tendons and equally unfit for adequate nerve growth. While sporadic nerve fibers can be

found in the crevices of such grafts,[140] this fact should not be overrated,[67] and the misleading practice of publishing pictures of such finds as evidence of "successful" regeneration[59] should be abandoned. Such trickle of fibers as is present in these cases is apt to be functionally irrelevant, particularly as many of the fibers passing through dense tissue are in danger of being pressure-blocked.

It seems that the ratio between solid and liquid content of tissues has not been properly recognized heretofore as constituting a limiting factor in neurotization. Its recognition makes it imperative to see to it that the union tissue forming between nerve stumps maintains proper liquidity. Provisions to this end will be outlined below.

Nerve Fiber Branching. Fibers have no intrinsic tendency to branch. Branching occurs always in response to local conditions of the environment.[177,185] It may occur terminally, that is, at the growing tip, or collaterally, that is, along the stem of a fiber.[143,144] Terminal branching presupposes, first, forking of the fiber tip, and second, continuation of growth along both branches of the fork. The former is a function of the pathway structure, any branching point of which may call forth the extension of filopodia in both directions. If both branches are successful in drawing supporting inflow of axoplasm, the divided flow may produce permanent twinning; if the competition is unequal, the winning branch will proceed and absorb the weaker one. Collateral sprouts have been seen to arise at points where a fiber has been exposed to mechanical or chemical irritation.[127,144] These sprouts have a better chance of growing if the growth of the main fiber stem is blocked, comparable to the taking over of the growth dominance by side branches in decapitated trees. Statistically, the incidence of branching will be proportional to the abundance of crossings in the pathway structure, which varies inversely with the orderliness of the latter. The more confused the substratum, the more profuse will be the branching of nerve fibers entering upon it. This explains the excess of branches in nerve scars and neuromas. Along well oriented and unobstructed structures fibers advance without branching, the growing tip apparently consisting of a single filopodium. The branching of Schwann cell cords in the glioma seems to follow similar rules.[200] The systematic ramification of regenerating axons in skin and muscle is partly guided by the pattern of the preserved degenerated branches of the original supply,[21] although occlusion of tubes may cause omission of some branches.[206]

Fiber Resorption. During the early phase of the regeneration process self-amputation and withdrawal of young and short fiber branches is common.[21,145] Concerning the later resorption of already established fiber branches, or even whole fibers, however, very little is known.[41] There has been much speculation as to the possible reduction of "functionally inadequate" fiber connections[205] (e.g. those producing "axon reflexes"), but tangible evidence to support that assumption is still lacking. Some slow regression in human amputation neuromas has been reported, but the majority of use-

less branches survive many years without change.[41] Experimental results with peripherally unconnected fibers confirm the durability of regenerated axons irrespective of their peripheral connections.[201]

Volume of Reinnervation. By this is meant the number of branches actually attaining peripheral connections, expressing the degree of completeness of reinnervation of receptor and effector organs. It depends on the following factors[195]:

(1) Size of the fiber source in the proximal stump.

(2) Amount of branching in the scar. Such branching can amplify the proximal source.[31] A given muscle or skin area might thus be saturated with nerve branches from a nerve smaller than that which had furnished the original supply.[39,103,181,198] However, the clinical exploitation of this fact,[18] recommended by Dogliotti,[39] remains problematical in view of certain complicating features,[4,195] which may offset the advantages of stepped-up branching.

(3) Number of fibers admitted into the peripheral stump. If sufficient time is allowed for regeneration, the number of regenerated fibers in the distal stump approaches more closely the normal fiber quota of that nerve than could be expected by mere chance.[35,63,103] When a distal nerve stump is confronted with an overabundant supply of nerve branches, it admits only a restricted number roughly corresponding to its own original content.[196] Perhaps the capacity of the distal stump diminishes with increasing delay of reinnervation.[82] Just how the distal stump controls the volume of neurotization, remains to be determined. Since fibers regenerate both inside and between old tubes, and often several to a single tube,[21,82,119,196,205] the number of degenerated tubes cannot represent the limiting factor. However, the fact as such is clear and condemns to failure attempts to force into a nerve significantly more nerve fibers than it can hold. It is interesting to note how many basic facts of nerve growth such as the one just outlined have been ignored in the devising of such methods of nerve repair as nerve flap transplantation, nerve implantation, etc., now outmoded.[8,130,155]

(4) Number of fibers persisting. This implies the possibility of secondary resorption of some fiber branches after they have grown through the distal stump.[21,205] To what extent this occurs, and whether as a result of spatial, nutritional, circulatory or functional inadequacies, is still obscure.

(5) Density of terminal connections. The capacity of a tissue to receive functional nerve supply seems to be strictly limited. Spatial conditions permitting, any number of nerve fibers may be crowded into an organ. But from that pool only a limited number of endings will be admitted to form functional connections passing impulses. A muscle fiber, in general, accepts only a single nerve branch and then insulates itself against further innervation.[46,55] For skin, likewise, there seems to be a definite saturation density beyond which innervation cannot be driven. This is indicated by the fact that as soon as a skin district is denervated, collateral supply from the sur-

rounding zone moves in,[147,175] presumably because of the cessation of some restraining action previously exerted by the area's own supply. In view of these facts, surgical attempts at "hyperneurotization"[48] of muscle can serve no useful purpose.

Maturation. In nerve regeneration, as in ontogeny, the outgrowth of the axon is only the first of a series of developments leading to the formation of a mature nerve fiber. Further elaborative developments include the realignment of sheath cells, myelinization, formation of nodes, increase of fiber diameter, and such functional adaptations as may occur after peripheral connection has been established. Common experience indicates that a regenerated nerve never resumes the precise features of a normal nerve. This holds for the nerve fibers as well as for the accessory constituents. Endoneurial cells and Schwann cells remain present in excessive numbers, the endoneurial connective tissue assumes relatively more space, the nodes of Ranvier are more irregularly spaced. Of more significant bearing on the restoration of function is the question of the restitution of the normal fiber size spectrum. Some functional imperfections as a result of incompletely recovered fiber size may be anticipated[205] from the known correlation between fiber diameter on the one hand and conduction velocity and associated physiological properties of the fiber on the other.[49] However, it has never been actually determined how serious such imperfections are, particularly in comparison with the much more profound disturbance of functional relations caused by the intermingling and consequent misconnection of fibers with other than their original end-organs.

The growth in width of the regenerated part of a nerve fiber occurs gradually,[134] and apparently progresses in proximo-distal direction.*[67] The normal size range may be approximated, but grouping into different size classes is less distinct than in normal nerve.[13,67] The caliber which will finally be attained is determined by no single factor. The original size of the fiber, the peripheral channel into which it grows, the number of branches, the nutritive conditions, the mode of peripheral connections, all these may influence the result. The distal parts of fibers which have regenerated through a constricted zone, for instance, remain thin and atrophic.[202] Evidently, continued expansion of distal fiber portions requires continuous supply of some growth prerequisites from the nerve cell body; and when this supply is throttled by a local constriction of the axon, growth of the part lying distal to that point will be impaired.

This fact can explain why large fibers regenerating into small distal tubes tend to remain undersized,[82,121] while small fibers entering large tubes do not expand to the large size of the latter.[121] In either case the dimensions of the tube would be the limiting factor: in the former, the distal tube would

* Unpublished oscillographic studies of regenerating rat nerves (carried out jointly with H. Davis and H. Maylander) have demonstrated a gradual decline of impulse velocity, and hence, fiber diameter, along the regenerated distal portion of a fiber.

resist expansion,[82] in the latter, the proximal tube would limit the supply to the distal portion. Moreover, growth pressure may reasonably be assumed to be the lower, the smaller the cell body exerting it. The size of fibers advancing endoneurially between tubes may similarly be determined as the resultant of growth pressure and peripheral limitations of space, nutrients, etc. Secondary atrophy, i.e., shrinkage without disintegration, may occur in fibers which have failed to effect peripheral connections,[201] but the evidence is still meager.

Myelinization has been shown to be a property of the neuron, although myelin cannot be produced except with the collaboration of the Schwann cell.[143,144] Whether the regenerated portion of a fiber does or does not acquire a myelin sheath, depends, therefore, on whether its stump of origin is myelinated or not. Myelinization of fiber parts whose growth has been impaired, remains poor.[61,202]

Specificity of Fibers. The problem of whether fibers can return selectively to their old periphery has remained controversial, in spite of considerable experimental treatment. Functional selectivity in regeneration has sometimes been claimed without clear commitment as to where and how it operated. It might operate (a) by restricting the ingrowth of nerve fibers to tubes of the corresponding type only; (b) by governing the establishment of peripheral connections; (c) by causing inappropriate connections to be dissolved; (d) by modifying the central relations of a misregenerated neuron.

Experimental and clinical evidence contradicts specificity within the major divisions of the peripheral system, inasmuch as any motor fiber is known to regenerate with equal ease into any motor nerve—witness the common crosses between the hypoglossal or spinal accessory and the facial nerve—and the analogous is true of the sensory system. As the functional implications of misregeneration are being made the subject of an extensive review under preparation, the problem need not be discussed here further.

The case is not equally clear with regard to the cross regeneration of motor into sensory channels and *vice versa*. Sensory-motor cross connections can be achieved experimentally,[20,178,179] but whether and to what extent their occurrence in normal regeneration is restricted,[15] either by differential facility of growth (contact specificity) along homologous and non-homologous pathways or by selective resorption of non-homologous terminal connections, is still a matter of conjecture. Penetration of motor fibers into sensory pathways and *vice versa* is undesirable mainly because it wastes part of the limited neurotization space of the distal stump on functionally useless elements.[160] Although antidromic impulses—afferent in motor fibers,[104,105] efferent in sensory fibers[10]—appear as by-products of normal nervous activity, it is doubtful whether they have the proper characteristics to act as sensory or motor excitations in the case of crossed end organs. Consequently, even if the random mixing of motor and sensory pathways in regeneration should prove to be of general occurrence, it would cause no conspicuous functional disturbance.

Trophic Restoration. A discussion of the regression of the denervated tissues and their recovery during reinnervation is beyond the scope of this survey.

Functional Restoration. This implies not simply the reconnection between the central nervous system and the receptors and effectors, i.e., recovery of general sensation and motility, but the recuperation of discriminative functions, i.e., proper discrimination and localization of sensory stimuli, and coordination of muscular activity. The literature on this subject is copious, yet contradictory and inconclusive. Its major deficiencies are lack of standard criteria in the assessing of functional recovery and often failure to take into full account the complexity of functional changes attending denervation and reinnervation. In the motor sphere alone, hypothetical "central reorganization" has often been credited with improvements of motor performance that were obviously due to trick movements, changes in muscle balance, compensatory contraction of unaffected muscles, mechanical transmission of pull, etc. It is difficult to tell from the conflicting evidence how much actual reorganization the centers can accomplish, when confronted with situations in which the majority of neurons have entered into new and unpredictable terminal connections.

A comprehensive discussion of these problems will be presented elsewhere. For the time being, it may be stated that the more critical reports on function after experimental and clinical nerve regeneration indicate a rather limited capacity for "reeducation" of misregenerated fiber connections.* The idea that the regulatory powers of the central nervous system, with or without conscious effort and practice, are great enough to make new and orderly impulse patterns emerge from a system of utterly confused connections, finds no support in known facts. A special kind of reconditioning which new peripheral relations produce in the nerve centers of embryonic or larval animals,[180,184] apparently disappears in the course of development[148,149] and has therefore (contrary to an earlier assumption[180]) no bearing on the clinical situation. In general, the more aberrant the morphological pattern of regeneration (owing to branching, straying, and shunting to the wrong endings), the less orderly will the functional activities be after recovery. And if one considers the mechanics of nerve regeneration, one realizes that full restoration of normal function, as it existed prior to the injury, is wholly beyond attainment. Only statistically can one try to approach this goal by taking measures that will allow the maximum possible number of nerve fibers to restore connections of the old type or, at least, one functionally similar. The recommendation of some neurosurgeons to match the fascicular topography of the stumps in suturing as best as feasible,[173] thus seems to make good sense physiologically. It is partly invalidated by the practical difficulties of identifying the orientation of dislocated stumps, of recognizing their fascicular pattern, and of suturing accurately without distortion; moreover,

* Compare, for instance, the articles by Ford and Woodhall[52] and Coleman.[33] An extensive bibliography will accompany the forthcoming review by Sperry.

the greater the gap, the less physiological congruity will there be between the cross sections because of the existence of intraneural plexuses.[155] However, the main factor to offset even the most careful matching of stumps is the profuse straying and branching of the regenerating fibers in the suture scar, and unless this can be avoided, there is no sense in trying to coapt the stumps macroscopically.

The Interdependence of Regeneration Phenomena. The survey of nerve regeneration presented in the preceding pages, even though highly condensed, conveys an idea of the complexity of the processes involved. The functional restoration of a nerve is a composite product of many and diverse interlocking phenomena, and no one of them can be singled out as the master key to the control of the others. While the orderly restitution of the axon remains the central objective, this cannot be attained except in the proper setting, which, in turn, depends on the behavior of the other tissue components. The more our knowledge of this intricate interdependence grows, the more judiciously shall we be able to deal with the practical problems of nerve repair. For example, certain measures that might be devised to stimulate the growth rate of nerve fibers might turn out to promote even more an obstructive fibrosis so that the net effect on nerve restitution would be adverse. Or one might try to amplify an undersized nerve source by causing the fibers to branch profusely during regeneration,[18,39] only to find out eventually perhaps that the number of branches any one neuron can maintain in good functional repair is limited. Numerous similar examples could be cited to illustrate that no single step of nerve regeneration can be viewed as an isolated entity. The intimate interrelationship among the various steps is a reality which one can ill afford to neglect in the practice of nerve repair.

METHODS OF NERVE REPAIR

Measures of nerve repair can accomplish their ends only to the extent to which they conform to the realities of nerve regeneration. In the light of these realities, as we now know them, many successful empirical procedures of the past find a splendid *ex post facto* justification, while, conversely, many past failures can now be traced to the fact that some peculiarities of the tissues involved or some of the subtle interrelationships just mentioned had been disregarded. It has become fairly plain by now that there can be no physical or chemical agent, no manipulation or drug, that would be universally beneficial to all component processes of nerve regeneration alike. What aids one, may hamper another. Any method of nerve repair will, therefore, have to be examined in all its consequences, and rated according to the balance of the good and harm it does. Only by wisely improving this balance sheet, can nerve repair be improved, by small steps, insignificant perhaps individually, but telling in their cumulative effects.

The capacity of a nerve to regenerate is subject to constitutional biological limitations. As in other tissue systems, the growth potential is determined by the properties of the tissue itself,[182] and growth rate cannot be

raised above a certain maximum. This need not apply to the purely physical part of the elongation of the regenerating nerve fiber, the rate of which is limited only by elasticity, viscosity, and the like. It does apply, however, to assimilatory growth which supplements and supports the elongation. Therefore, if mammalian nerve fibers have never been seen to exceed a daily rate of free advance of about 4 mm. at best,[65] this presumably defines the maximum output of which they are capable under optimal conditions. Whenever recoveries at much faster rates are reported, there is reason to suspect either that the nerve had not been severed or that nerve sources closer-by had substituted.

Methods of nerve repair must, therefore, aim not at "stimulating" nerve growth, but at providing it with the conditions under which it can best realize its own potentialities. In last analysis, it is the nerve that has to do the repairing. All we can do is facilitate the job by supplying the necessary prerequisites, and by keeping out handicaps. In view of this situation, it is not surprising that attempts at "stimulating" nerve growth directly have had no success in the past. Particularly, the claimed stimulating effect of the Vitamin B group[162] and biotin[68] has not been substantiated in critically controlled experiments, either *in vivo*[50,101] or *in vitro*.[27,29] While nerve regeneration under thiamin deficiency may be impaired,[28,108] thiamin excess does not produce excessive nerve growth, although it does seem to facilitate recovery after central lesions,[174] which involves no growth. There seems to be little hope of doing much for nerve regeneration along that general line. At present, it seems that the only way in which nerve regeneration can be effectively promoted is to avoid the natural and clinical hazards that tend to depress it.

Concerning the natural hazards, it must be borne in mind that the general wound healing tendency of the body, by leading to cicatrization, happens to run counter to what would be in the best interest of nerve healing. Part of the surgical effort must, therefore, be devoted to eliminating this conflict. This can be done (a) by holding scar-provoking factors to a minimum, and (b) by directing the unavoidable remainder into a course where nerve restitution will be harmed least, for instance, by forcing scar tissue to grow along, rather than into, the nerve. A nerve scar not only distracts and bars nerve outgrowth, but also is apt to interfere with subsequent maturation and impulse conduction in regenerated fibers. Its avoidance thus becomes a matter of prime concern and has always been recognized as such by the surgeon. Yet, the surgical intervention in itself may intensify rather than alleviate the condition. Trauma, introduction of foreign suture materials, infection, and hemorrhage affect the volume of the scar, while the stress pattern at the junction determines its prevailing orientation. Both must be taken into account.

The perviousness of the distal stump to regenerating fibers may fluctuate within wide limits, with pressure, past history of Wallerian degeneration, vascularization, macrophage activity, and perhaps stretch, being the major

variables. Depending on the condition of the distal stump, the rate and volume of nerve fiber regeneration will vary, which in turn will determine how soon and how well the muscle will be reinnervated.

Escape of fiber branches at the suture line will not only produce painful neuromas, but may, if excessive, drain the growth potential of the whole nerve and thus reduce its capacity for functional recovery. The point that such fiber escape should be precluded is therefore well taken.

These examples may suffice to illustrate our contention that the way to improve nerve repair is not by trying to "stimulate" nerve growth, but by eliminating the handicaps which would ordinarily be in its way. These handicaps operate on a microscopic rather than macroscopic plane, and we can avoid them only after we have learned to recognize them.

SUTURELESS TUBULATION

Reunion of severed stumps by means of a fitting cuff of artery or other suitable material without the use of sutures has certain unique advantages for nerve regeneration, which other methods do not provide to an equal degree. This method, referred to for brevity as "tubular splicing" or "sleeve splicing," has thus far been tested in laboratory animals only, but the lessons of the experiments are unquestionably applicable to clinical practice. The experiments, which have been described in detail elsewhere,[186,189,193,200] will be reviewed here only briefly. However, some supplementary information not otherwise published will be added.

The main purpose and effect of sleeve splicing is to prevent the formation of a "suture line." Ordinarily, the suture line represents a zone in which the organization of the nerve is definitely and permanently abnormal. Here the nerve fibers are forced to branch profusely and to stray and commingle at random, with the consequences outlined above, while fibrous tissue penetrating from the sheath and from extraneous sources may make the link so compact as to interfere with growth, maturation, and perhaps conduction, of the regenerated fibers. In contrast, the union tissue of sleeve-spliced nerve stumps assumes the same organization as the rest of the nerve, so much so that in successful cases the transition between the former stumps is perfectly smooth.

Sleeve splicing owes its success to three main facts: (1) absence of sutures; (2) transmission of tension between the stumps and the newly forming union tissue; (3) confinement of fluid within the gap and the union tissue. A thorough histomechanical analysis[200] of the healing process after end-to-end union with and without tubular splicing has demonstrated that if the tissue linking the nerve stumps is to become a well organized nerve segment, rather than a scar, longitudinal stress and high liquid content are indispensable prerequisites.

This may be explained here briefly by the example of an arterial splice, supposing that we are dealing with a case in which the nerve stumps can be closely approximated without stretch. The nerve ends are joined by placing

them inside a fitting cuff of artery. The cut surfaces are not brought in contact but are left separated by a gap of a few millimeters, which becomes filled with blood. During the days following the operation, this blood clot undergoes a remarkable transformation, the course of which is of crucial importance for the outcome of the ensuing processes of nerve regeneration. The following events occur in rapid succession[200] (Fig. 5).

(1) The fibrin of the blood clot in the gap fuses firmly with the nerve stumps (Fig. 5, *1*).

(2) The erythrocytes of the clot disintegrate, leaving a spongy fibrin framework with liquid-filled meshes behind (Fig. 5, *2*).

(3) The clot detaches itself from the wall of the sleeve, while firmly stick-

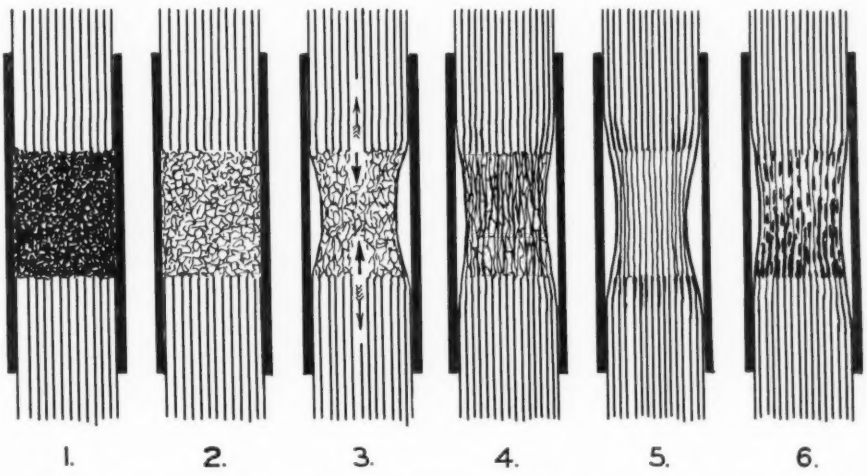


FIG. 5. Transformation of the union tissue between sleeve-spliced nerve stumps. The illustrated phases of the process represent operative, rather than chronological, steps. Chronologically the various phases overlap. *1*, Blood clot in gap. *2*, Fibrin formation. *3*, Lateral detachment of union tissue; syneretic shrinkage of clot (plain arrows) and traction from stumps (feathered arrows) lead to longitudinal tension. *4*, Tensional orientation of the fibrin network (corresponding to Fig. 4, *A* and *D*). *5*, Liquefaction of unstretched fibrin. *6*, Outgrowth of sheath cells and axons through the oriented fibrin matrix.

ing to the nerve ends (Fig. 5, *3*). It thus constitutes a mechanical link between the stumps and hence becomes subject to longitudinal traction. Any tension acting on the nerve transmits itself directly to the clot. Similar stresses arise in the clot from the shrinkage attending its syneresis.

(4) These longitudinal stresses act in the manner described above for stress patterns in general. They force the fibrin elements into a predominantly longitudinal orientation, resulting in the formation of straight fibrin threads which span the gap from one nerve end to the other (Fig. 5, *4*, *5*).

(5) Fibrinolytic enzymes, liberated presumably from disintegrating leukocytes and possibly also exuded from the nerve stumps, destroy all

finer cross links of the fibrin reticulum, while sparing the heavier, longitudinally oriented threads (Fig. 5, *5*).

Through this chain of processes the nerve stumps become reconnected within less than a week by a system of straight parallel fibrin strands. Except for these threads, the space of the former gap is still filled with fluid, partly fibrinolysate, partly perhaps nerve exudate,[187] which the impermeable sleeve prevents from dissipating.

It is in this setting, then, that the outgrowth of sheath cells, axons and capillaries takes place. As these elements are bound to move along the existing solid-liquid interfaces, the fibrin threads serve them readily as climbing ropes (Fig. 5, *6*), and since the latter span the original gap in straight lines, the most direct and unconfused transit of the regenerating nerve fibers and accessory tissue components from stump to stump is made possible. As a result, the outgrowing fibers and cells glide over the fibrin rails of the union tissue with great ease, thus retracing the parallel longitudinal lines of the fibrin pattern which, in turn, are a product of the prevailing mechanical stresses. The abundance of interstitial liquid, on the other hand, insures ample space for the advancing tissue mass in the sense indicated previously.

As one can see, the effects of sleeve splicing on subsequent nerve regeneration are subtle and manifold. Specifically the following features stand out.

(1) By insulating the junction, the sleeve prevents the young union tissue which fills the gap from adhering to any structures but the nerve stumps themselves.

(2) By the tensions transmitted directly from one stump to the other through the union tissue, the latter is molded into parallel fiber strands corresponding to, and continuous with, those of the nerve stumps.

(3) This pathway system is free from obstructions, and interlacing of its elements remains at a minimum. Consequently, neither the regenerating axons nor the sheath cell cords are subject to the extensive branching and straying typical of ordinary nerve scars.

(4) The longitudinal organization of the union tissue directs the growth of the intraneural blood vessels straight across the gap and thus effects prompt vascular reconnection between the stumps.

(5) Fibrous connective tissue surrounding the nerve is likewise forced into a longitudinal course, where it develops into a useful sheath around the junction, instead of penetrating into the interior, where it would deflect and block nerve fiber growth.

(6) By suppressing the formation of communications between the inside of the nerve and the surrounding tissues, the sleeve not only precludes the intrusion of extraneous scar tissue into the nerve, but also the escape of regenerating fibers (neuromas) and sheath cells (gliomas) from it.

(7) Acting as a tight container for the liquid in the union tissue, the sleeve insures the necessary space for the passage of nerve fibers in adequate numbers and for their later unimpeded lateral expansion.

(8) Owing to the straightness and parallel arrangement of the guide lines, the regenerating fibers traverse the gap in essentially the same assemblage in which they emerge from the proximal stump. Hence, functional grouping, as far as it is expressed in topographical grouping, is at least partially preserved, in contrast to its complete disruption at ordinary suture scars.

In order to evaluate the method of sleeve splicing, and as a possible guide for further advances in the technique of nerve reunion, it seems advisable to

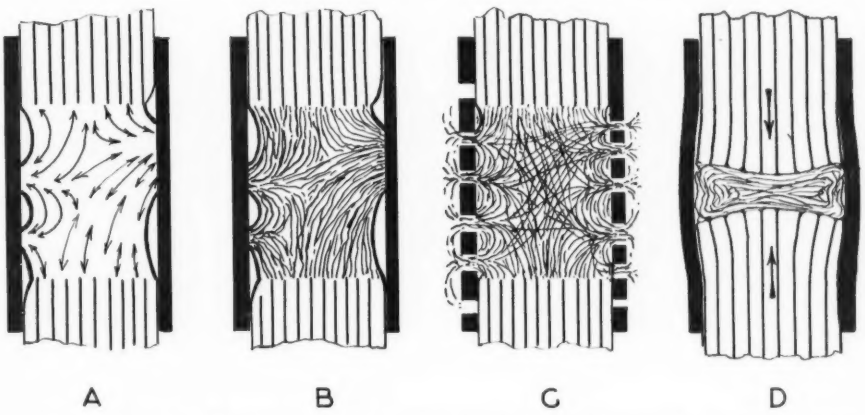


FIG. 6. Examples of disorganization of the union tissue. *A*, *B*, Stress pattern (*A*) and resulting structure of the matrix (*B*) after incomplete lateral detachment of the union tissue from the sleeve wall. *C*, Distorting effect of pores or holes in the sleeve wall. The tissue is drawn toward the breaks. *D*, Transverse orientation of the matrix as a result of pressure from the nerve ends (arrows).

assess the various features listed above critically in regard to their significance for final functional restoration. While the contrast between the orderliness of a sleeve-spliced union and the confusion at junctions effected by other means is spectacular, this does not in itself prove the superiority of the former over the latter in practical respects. The following point-for-point discussion aims to facilitate a comparison of sleeve-splicing with other methods. (The various points will be dealt with in the order of the above listing.)

1. Insulation. To insulate a suture line against ingrowth of fibrous tissue, has been the purpose of many wrapping and tubulation attempts of the past (see below). In many cases, these attempts were half measures in that the resorption or perforation of the materials used failed to provide more than perfunctory insulation. The sleeve as used in sleeve splicing does not operate so much as a mechanical shield as by creating conditions which will force scar growth into a longitudinal instead of transversal course. Even though a closely fitting sleeve precludes the intrusion of extraneous tissue,

the epineurial sheath inside the sleeve is an ever present source of fibrous tissue, and if it fails to cause trouble in sleeve-spliced nerves, this is because the longitudinal stress pattern diverts the proliferated material into a longitudinal course along the surface of the nerve. Accordingly, any intervention or postoperative occurrence that upsets the longitudinal stress pattern is bound to defeat the purpose of shielding.

Most common failures of this kind arise from adhesions between union tissue and the covering cuff (Fig. 6A, B). Such adhesions produce tension lines directed from the surface into the interior of the gap; hence, they lay down direct inroads for the penetration of epineurial tissue into the nerve (Fig. 6B). The inner lining of the cuff must, therefore, be of such a nature that the blood clot will either not adhere to it from the very first, or, at least, become detached shortly after by fibrinolysis. Arterial tubes satisfy this condition. So do sleeves of tantalum metal,[193] the use of which will be described below. On the other hand, coverings made from materials capable of fusing with the fibrin of the blood clot would fail in this respect.

It is equally futile to expect a longitudinal stress pattern to develop after sheathing the union with cuffs that either are porous or, though initially tight, undergo rapid erosion and resorption (Fig. 6C). Any hole or fissure in a sleeve is apt to become, first, an anchor point for the stress pattern; secondarily, a center upon which fibrin fibers will converge; and ultimately, an entrance point for extraneous connective tissue as well as an escape route for regenerating sheath cells and axons. Materials sufficiently resistant to withstand resorption for several weeks may, however, be acceptable; for during that period the union tissue will have assumed its longitudinal orientation, a continuous fibrous sheath will have covered the junction, and after the sleeve has thus served its purpose, it may be dispensed with.

For similar reasons, a coat of blood plasma such as is used in the so-called "plasma suture",[64,207] of nerve cannot be expected to serve as a real sleeve in the sense here emphasized For the surface coat of plasma and the blood clot in the gap are bound to merge into a single mass, particularly as some suture plasma is apt to seep in between the cut surfaces. The syneresis of such an irregular mass will produce an irregular tension pattern, leading to corresponding irregularities of the subsequent nerve and scar growth. The marked contrast in microscopic appearance between junctions after plasma suture and after sleeve splicing bears out this contention.*

In conclusion, only if there is no adhesion between clot and sleeve, can a strictly longitudinal tension pattern develop.

2. Tension. Mechanical considerations intimate that the most potent factor in the creation of tensions at the junction is the syneretic shrinkage of

* A semidiagrammatic illustration of a number of suture lines after plasma suture may be found in the article of Gutmann and Sanders[67]; for illustrations of sleeve-spliced junctions, see the figures in Weiss,[186,189,190,193] and Weiss and Taylor.[199,200] An improved picture of a plasma union was presented by Tarlov[165] at the 1944 meeting of The Harvey Cushing Society.

the clot itself. If the nerve stumps are sufficiently taut to resist the contractile tendency of the clot, the desired longitudinal stresses arise in the latter. No such stresses can be expected between slack nerve stumps. From these facts two postulates can be derived. First, there should be a small blood clot between the nerve stumps not only as a cementing agent but primarily as a foundation for the union tissue, to orient the fibrin bridge between the stumps by its syneresis. Second, the nerve stumps must not be allowed to yield to the contraction of the union tissue. Whether this latter provision requires that the union be placed under active tension, remains to be seen. It may be sufficient to keep the nerve just free from slack. The tendency of freshly transected nerves to retract after the operation will presumably place enough strain on the union tissue to produce satisfactory orientation. Older lesions will show less of this tendency, but even in these it may be unnecessary to apply more than just the gentlest stretch. Later, as the union becomes firmer, traction along the nerve may be allowed to increase as a means of accentuating the longitudinal organization of the union.

The optimal size of the blood gap is an empirical problem. Too short, its syneretic effectiveness will be low; too large, it presents increasing hazards to nerve fiber regeneration. The hundreds of cases thus far studied indicate an optimum length of approximately once or twice the diameter of the nerve. Even though successful regeneration through much larger gaps, filled with specially prepared blood, has been obtained (see below), the longer the gap, the less strict will be the tensional organization of the union tissue.

If the nerve ends are pressed against each other, with or without intermediary blood clot, the result may be serious. It has long been an empirical rule to avoid flanging of the nerve ends in end-to-end sutures.[8] The soundness of the rule becomes evident if one realizes that any axial pressure against the union tissue produces stresses directed at right angles to the nerve axis (Fig. 6D). The union tissue will therefore assume a prevailingly transverse orientation tending to deflect and stop the regenerating nerve fibers instead of guiding them lengthwise to the distal stump. Even if the nerve cross sections are not in immediate contact, but are left separated by a small blood clot, whenever they press toward each other, the result will be the same.[200] Obviously, it is the fate of many end-to-end sutures to create just this kind of pressure.

Sutures at the nerve junction, that is, stitches placed near the rims of the stumps, are objectionable for a variety of reasons, but their most serious defect is that they prevent the formation of a longitudinal stress pattern. Even if foreign body reactions can be wholly avoided by the use of inert suture material; even if the stitches can be strictly confined to the epineurium, and even if we disregard the fact that each thread or wire stitch represents a potential path of penetration for fibrous tissue and of escape for regenerating fibers, interference with the stress pattern is an unavoidable consequence of suturing. For one thing, the drawing together of the stumps

gives rise to that undesirable transverse pressure pattern just mentioned. Moreover, since all traction between the stumps is transmitted through the rigid suture threads, it bypasses the union tissue at the suture line and deprives it of the beneficial influence of longitudinal tension. The tensional chaos prevailing at a junction that has been protected by sutures against traction finds its visible expression in the disorganization of the resulting "suture line."

Therefore, from the theoretical as well as the experimental standpoint, omission of sutures near the cut surfaces of nerve stumps seems a prerequisite to optimal regeneration. In practice, forcible approximation of the stumps is often a necessity. However, this can still be effected without suturing at the very level of the junction, simply by placing stay sutures or sling stitches through the nerve stumps at such a distance from the ends that the junction itself remains unaffected. Only the excess tension on the stumps should be taken up in this way, leaving enough available for the free nerve ends to straighten the young union tissue in the gap (see below).

In conclusion, sleeve splicing can have the desired effect only if the nerve stumps are not slack and if the union tissue is enabled to act as the sole mechanical link between the stumps. This implies omission of any sort of rigid sutures between the nerve ends.

3. Growth Orientation. By aligning the fibrin strands lengthwise, the longitudinal stress pattern gives rise to two important effects: it prepares the shortest direct route across the gap for the outgrowing sheath cells and axons, and it removes a most potent incentive to axon branching, namely, intersections in the fibrin matrix. This fact is plainly evident in the microscopic pictures of sleeve-spliced nerves.[200] It is fully borne out by actual fiber counts, which have yielded substantially similar figures for the proximal stump, the region of the junction, and the distal stump.[186]

While sleeve splicing thus definitely reduces branching and straying of fibers to negligible proportions, the question remains as to how much significance one should attach to this fact. The answer will depend on how serious a drawback to nerve regeneration profuse branching and straying of nerve fibers at an ordinary suture line really is. That it may affect functional restoration, will be shown below. What concerns us here is whether it affects morphological repair of the nerve.

The problem can be treated only in statistical terms. If regenerating axons remained unbranched, the proportion of fibers reaching the distal stump would be inversely related to the frequency of diversions in the scar. On the other hand, since intersecting pathways also increase the incidence of axon bifurcation, loss by diversion might be compensated by amplification of the fiber mass by branching. Nerve regeneration as a whole might, therefore, suffer no net numerical loss, provided that all axon branches possess the same power of growth, no matter how many of them there are to a single neuron. However, there is good reason to doubt this premise. While our factual information on this point is still very fragmentary, numerical studies

on nerve regeneration,[195] as well as the realization that the axon grows essentially by synthesis from the cell body,[82,202] seem to indicate that the growth energy of a neuron is not unlimited. Consequently, the vigor of growth of a branch which must share the limited resources of the neuron with a number of sister branches is likely to be less than that of an unbranched sprout. When, as occasionally happens, more than one branch of the same neuron reaches the periphery (e.g. in nerves showing so-called "axon reflexes") it is quite conceivable that such multiple branches may never grow to full size. Consequently, if a given neuron can support only a limited amount of axoplasm, the dissipation of a major fraction of it in the form of abortive branches in the scar would evidently stunt the growth of their sister branches that happen to proceed into the periphery. Such branches will presumably grow more slowly, be more easily arrested by obstacles, and retain small caliber.

In conclusion, the oriented pathway system produced by the longitudinal stress pattern is of dual benefit to nerve regeneration: in a positive way, by guiding sheath cells and axons across the gap; in a negative way, by reducing the incidence of branching and straying, which, statistically speaking, affect regeneration adversely.

4. Vascularization. The blood supply of peripheral nerves is furnished by a continuous system of anastomosing longitudinal vessels fed by arteries which enter at a few points along the course of the nerve.[2,12] In view of the continuity of the longitudinal neural vessels, any one of these collateral sources may be eliminated without harm to the nerve.[3] Therefore, the fact that a splicing sleeve over a nerve junction might permanently bar one such source from reentry into the nerve is wholly irrelevant. The union tissue can derive abundant vascularization from intraneural channels and does not require local extraneural contributions. On the contrary, where local ingrowth of blood vessels occurs, as, for instance, in many unshielded junctions, it is frequently attended by fibrosis and strong adhesions. Moreover, it has never been established whether or not in such cases a direct vascular reconnection between the severed nerve stumps is effected, nor can the possibility be ignored that lack of vascular continuity might under certain circumstances impair nerve function.

In contrast, sleeve splicing facilitates vascular reconnection between the stumps. When invading the union tissue, the vascular sprouts join the other regenerating elements in assuming a predominantly longitudinal course.[200,201] Circulation between the two stumps is thus restored promptly, sometimes within a matter of days.

5. Prevention of Scars. Ingrowth of scarifying connective tissue has often been stressed as impeding the advance of regenerating nerve fibers. But while the disorienting effect of the scar during the earlier regeneration phase is a definite handicap, its progressive condensation and contraction during later phases introduces even more serious difficulties by tending to strangle those nerve fibers that have passed through. As was mentioned above, local

constriction of a nerve makes it impossible for those parts of the nerve fibers distal to the affected level to regain proper caliber and myelinization.[202] Such underdeveloped fibers are not necessarily unfit for functional use, as regenerated fibers generally resume functional activity long before they have fully matured.[67] However, again in statistical terms, recovery may be assumed to suffer in proportion to the weakness of the fibers. Moreover, excessive scar contraction is apt to produce pressure block of conduction through the strangled region.

In conclusion, by deflecting scar tissue into a longitudinal course, where its contraction cannot encroach upon the nerve, sleeve splicing eliminates a serious hazard.

6. Suppression of Neuromas and Gliomas. Nerve fibers and Schwann cells moving into a random scar are not stopped short but may keep on roaming for some time without direction, giving rise to the bulging terminal neuromas of the proximal stump and gliomas ("schwannomas") of the distal stump. The character of these swellings depends largely on the accidental configuration of their environment. If the scar tissue is frayed and radiates into the adhering tissues, nerve fibers and Schwann cells escaping from the nerve ends will infiltrate the surrounding parts. Where the nerve ends have become capped by a fibrous layer, and particularly when edema fluid has accumulated, the trapped nerve fibers are forced to keep circling inside.[187] Either mode of distraction leads to two undesirable effects: hyperaesthesia or pain at the site of the neuroma, and dissipation of nerve fibers which would otherwise be available for regeneration.

Fiber counts of regenerated nerves from which fibers have escaped during the passage from the proximal into the distal stump[195] have shown that such losses are irretrievable and may lead to a corresponding deficit in the peripheral reinnervation. Unprotected suture lines offer opportunities for such fiber escape, not in the crude manner in which it is sometimes stated, by leaving "holes" open for the exit of nerve fibers, but because they favor the formation of fibrous and vascular connections between the interior and exterior of the nerve. As was stressed before, nerve fibers do not grow through openings as such, but only along solid supporting structures. A suture line may, therefore, be macroscopically faultless, with the epineurium tightly closed all around the nerve, and yet, the connective-tissue strands and vessels which will penetrate along the suture threads and between the apposed rims of the epineurium will establish escape routes from the interior. To prevent fiber escape becomes, therefore, a matter of preventing the formation of pathways linking the inside with the outside of a nerve. A splicing sleeve serves this purpose provided it is and remains unperforated and impervious to connective tissue until the union tissue has become organized and the mass of regenerating fibers has passed the critical level. The same considerations apply here as discussed above under point (1). Sleeves from materials undergoing rapid resorption will be no insurance against local fiber escape unless they can force the replacing connective-tissue elements to array themselves

longitudinally so as to form a hermetic sheath around the nerve. What counts in this case is the microscopic organization, not the macroscopic appearance of the sheath.

The suppression of Schwann cell overgrowth in sleeve-spliced nerves is remarkable. It seems that Schwann cell cords growing forth from the cut ends of a nerve tend to proceed until they meet other Schwann cells and then stop. Chances of encounter are obviously lower in the tangle of a suture scar than along the straight rails of a sleeve-spliced union. Therefore, Schwann cell proliferation is excessive in the former case, while in the latter it stops after repopulating the straight lines of the union tissue.[200]

In conclusion, sleeve splicing, properly executed, does benefit nerve regeneration by preventing fiber dissipation at the site of the lesion.

7. Confinement of Liquid. The necessity of according regenerating nerve fibers sufficient space in which to expand was stressed above. The transformed (degenerated) distal stump provides space approximately equivalent to its own original fiber complement. With an increasing period of denervation, it shrinks[82] and becomes correspondingly less favorable for neurotization. Even with this limitation, spatial conditions in the distal stump are essentially adequate. This is not necessarily true, however, of the union tissue between the stumps. Originally, the liquid content of this tissue is high,[96] fed by syneresis, hemolysis, fibrinolysis,[200] and endoneurial fluid.[187] However, unless this liquid is prevented from oozing out, the solid constituents at the junction will become increasingly denser, occupying more and more of the space that should be kept open for the passage and later expansion of nerve fibers. Thus, even without intrusions from extraneous sources, the tissue at the junction would act like a scar, that is, contract and impede fiber growth.

In conclusion, by providing for the retention of fluid in the young union tissue until the nerve has become reconstituted, impermeable sleeves perform a distinct service to regeneration.

8. Functional Reorganization. Functional order, i.e., motor coordination and sensory discrimination, can be restored only to the extent to which either the process of regeneration brings fibers back to their own old terminations or the central nervous system can adjust its functions in accordance with the new pattern of connections. As the former condition is practically unattainable, functional recovery must rely largely on functional readjustments (see above). Critical observers describe the scope within which these can be achieved as rather limited. Much will depend on how much of the original orderliness of the peripheral nerve fiber pattern can be preserved during regeneration. Even though most fibers will end at new terminations, there may be a distinct advantage in leaving them at least assorted in groups, on the premise that it should be easier for a given central cell mass that used to act as a unit to change its functional role as a whole, than for it to reassign to each one of its elements a new role.

While the criss-crossing of fibers at ordinary suture lines dissolves all for-

mer functional grouping of the regenerating fibers, sleeve splicing permits them to retain some degree of their original associations. This has been proven both by histological[186,200] and physiological[189] studies of nerves regenerated after sleeve splicing: Individual fascicles of the proximal nerve have become reconnected with circumscribed muscle groups, proving that their fiber complement has remained essentially assembled during the transit into the distal stump.

In conclusion, greater orderliness of connections is rendered possible by sleeve splicing. On theoretical grounds, this should facilitate functional re-education.

The preceding discussion has outlined eight crucial features to which sleeve splicing owes its success. It should be remembered, however, that all conclusions are based on experiments in animals only. So far as these experiments go, the method has proved its value. Not only in small animals,[195] but

TABLE 2*

Specimen	Nerve	Graft	Splicing Artery	Time Months	Muscles	Weight			
						Operated Side (O) g	Control Side (C) g	Difference (O−C) g	Percentage Recovery
cat #3	tibial	+	f.-d.	6	gastrocn.	13.9	14.7	−0.8	95%
	peron.	+	f.-d.	6	peron.	5.7	6.3	−0.6	90%
cat #6	tibial	+	live	12	plantar flexors	36.5	38.5	−2.0	95%
	peron.	+	live	12	dorsi-flexors	16.4	16.7	−0.3	98%
monkey #21	tibial	−	f.-d.	6	plantar flexors	56.0	52.0	+4.0	108%

* The table lists all cases in which terminal muscle weights have been determined. "f.-d." is abbreviation for "frozen-dried."

in cats and monkeys as well,[189,190] have paralyzed muscles after reinnervation through sleeve-spliced nerves recovered nearly their full volume (in terms of the corresponding muscle of the control side), even with the interposition of a frozen-dried nerve graft (Table 2). Failures have occurred, but they could always be traced to faulty technique.[186] When properly executed, sleeve splicing yields sure success in all animal groups thus far tested.

TECHNIQUES OF NERVE REUNION

Artery Cuffs. The clinical success of sleeve splicing will depend on how closely its crucial features can be reproduced in the human subject, as well as on the readiness with which cuffing material of the proper specifications becomes available.

Arteries, while performing excellently in laboratory animals, may not be the final solution for human nerves. Some difficulties have been pointed out previously, one of which is that fresh arteries sometimes tend to tighten around the nerve so as to produce constriction.[186] This can be circumvented by subjecting the arteries before use to quick-freezing and drying. Nerves of rats, cats, rabbits, and monkeys spliced with frozen-dried and rehydrated arteries have, on the whole, shown excellent functional recoveries.[189,190] Frozen-dried arterial sleeves become permanently incorporated. They are just as elastic and handle just as easily as fresh arteries. The fact that they can be kept for many months in the dry state makes it possible to keep a store of assorted sizes on hand. Short rehydration is all that is needed to make a stored sleeve ready for use.

These advantages are partly offset by certain weaknesses. Adhesions between frozen-dried sleeves and their surroundings are more extensive than those of live arteries. Similarly, local adhesions between their inner wall and the union tissue are not uncommon, with the result that the otherwise straight pattern of regeneration suffers sporadic disturbances. Local erosions occur, and through such breaks an appreciable number of fiber branches may penetrate and get lost in the wall of the sleeve. While this need not affect the volume of regeneration, it might leave the junction clinically in a state of potentially painful hyperaesthesia. Moreover, there is still the supply problem to be considered. As the freezing-drying procedure does not abolish the biochemical species differential, only human arteries can be used. Aorta furnishes the most suitable sleeve, but only fetal or early infant aorta qualifies in point of size, and since the sleeve must be free of side branches, the yield from a single specimen is rarely more than three pieces. Other types of arteries are less desirable because of their heavy muscular wall.[186] Veins have proved too flabby, at least in animal experimentation.[186,189]

Tantalum Cuffs. It thus became advisable to look for a substitute for arteries, more easily procurable, without being less effective as a splicing agent. As will be shown below, none of the materials suggested in the past for nerve tubulization could qualify. The favorable results obtained recently with the surgical use of the metal tantalum,[25,132,152] however, pointed to a possible solution. Success came after a method was discovered[193] by which full elasticity could be conferred upon the otherwise soft and pliable tantalum foil. By proper heat treatment, the foil can be fashioned into fully resilient cylindrical rolls with overlapping edges. The overlapping parts stay in intimate contact by their own elastic pressure so that the tubes remain tightly sealed even though their width is adjustable within the limits of elasticity and friction.

Technically, such tubes can be applied for sutureless nerve reunion in much the same manner as arterial sleeves, provided the nerve bed at the junction is straight and can be kept straight during the healing process. Biologically, their performance is equal to that of arterial sleeves.[193] They are inert and provoke little, if any, foreign body reaction. As the union tissue

does not adhere to the metal, its longitudinal orientation is assured, while the epineurial and other potentially scar-forming tissue is forced to grow down along the inner wall, where it reconstitutes a smooth cylindrical sheath over the junction. Dissipation of fluid from the interior is prevented. No scar can form at the level of the junction. Vascular connection between the nerve stumps is restored promptly. If adequately executed, such unions show practically no trace of the former break as early as five weeks after the operation in cats and monkeys. There would seem to be no objection to removing the metal sleeves after this period if this should become clinically desirable.

The main shortcomings of tantalum sleeves are their rigidity, which limits use to straight-way unions, and their opacity, which removes the junction from direct visual control. The search for an even superior material, combining the features of tantalum sleeves with greater flexibility and translucency, will therefore have to be continued.

Special Uses of Sleeves. Aside from the fact that it provides an optimal setting for nerve regeneration, sutureless sleeve splicing has certain practical advantages of some consequence. The duration of the operation is considerably shortened as compared to conventional suturing. Furthermore, even nerves of the smallest caliber, too fine for accurate suturing, can easily be mended with sleeves. Where fascicular topography is recognizable, e.g., in freshly severed nerves, separate reunion of individual bundles can be effected with ease. Nerve lesions at branching points can be treated simply by placing the common proximal stump into one end, and the several distal stumps into the other end of a sleeve. Sleeve splicing, thus, not only simplifies the technique of nerve repair, but also makes repair feasible in cases that would defy other less subtle methods.

Sleeve splicing is of particular significance in connection with the use of nerve grafts for the bridging of large defects. Much of the blame for the failure of grafts can unhesitatingly be ascribed to the fact that they were improperly joined to the nerve stumps. If a single scarified suture line after end-to-end suture can impair nerve regeneration, two junctions are bound to be even worse.[11] The suggestion has been made to resect and resuture, in a second operation, the distal suture line.[36] It would seem preferable, however, to avert the formation of suture line partitions and scars in the first instance, a goal which can at least be approximated by sutureless sleeve splicing. As has been shown experimentally, sleeve-spliced nerve stumps become linked in the same orderly fashion whether they contain axons or not. Axon-free ("aneuritic") segments, such as a graft and the distal nerve stump, thus become joined by longitudinal cell strands which afford unimpeded passage for the regenerating axons when they later arrive at this level.[200] The conditions for strict orientation of the union tissue between graft and nerve stumps are not quite so favorable as between directly opposed nerve ends because of the unavoidable slackness of the graft. Even so, the experimental tests in rats,[199] cats and monkeys,[190] using frozen-dried nerves as grafts, have demon-

strated the adequacy of the sleeve-splicing technique in grafting. It also simplifies the use of cable grafts, as the multiple strands which are to make up the cable can be introduced one by one into the sleeve without further need of attachment.

The Problem of Gaps. The preceding discussion presupposes conditions under which the nerve ends can be brought and held within close range without force. This is not commonly attainable unless by special measures.[116] The length of the gap between the nerve ends is determined by the original loss of substance, subsequent elastic retraction of the stumps, and in secondary reunion, the length to which the fibrotic ends have to be resected. To gain the lost distance, mobilization and rerouting of the nerve course, extreme flexion of joints, progressive stretching, and even shortening of bones, are being practiced.[8,116,130,139,155] Of these measures those that do not require further stretching of the mended nerves are fully compatible with sutureless sleeve splicing. Where stretching becomes necessary, either at the time of the operation or after healing, the weakness of the link must be taken into account. In such cases, the customary suturing, even if not fully successful in shutting the nerve fibers in and scar tissue out, serves the very real function of holding the stumps in apposition.

Sleeve splicing does not of itself provide a substitute for this latter function, since sleeves must not be fitted too tightly, and hence, have only limited gripping power. Suturing of the nerve ends inside the sleeve, on the other hand, would cancel most of the benefits of the method. A solution has been found in the combination of sutureless sleeve splicing with a "remote" suture for holding purposes.[193] A single loop of thread or wire is stitched through both nerve stumps at points as remote from the ends as is technically feasible, and then drawn just tight enough to bring the cut surfaces within a few millimeters of each other. The free ends are then united by a sleeve as usual, and the syneresis of the blood clot and the slight "give" of the loop in the nerve are relied upon to allow the longitudinal stresses needed for the organization of the union tissue to develop. The tension loop is, of course, not to be enclosed in the sleeve, but to be left on the outside. Another way of securing the approximation of the stumps would be by separate stay sutures, but the former method seems preferable because it leaves the nerve mobile. The practical details of these problems remain to be worked out.

Data on two points, inadequately known at present, are indispensable for judicious action in nerve repair: the amount of stretch which nerve can tolerate without damage, and the maximum acceptable length of the gap between the nerve ends in a sleeve.

As for the former point, the clinical literature is inconclusive (see Sanders[139] for a review), as some authors approve of degrees of stretch certain to rupture nerve fibers and blood vessels, while others caution against even the slightest extension. Animal experiments have revealed the dangers of excessive stretch.[78,113,161] During the embryonic as well as the postnatal growth period of an individual, nerves are definitely under natural stretch, as they

are "in tow" by the growing organs.[185] This stretch, however, is exerted very gently and is distributed evenly over the length of the nerve. These conditions, notably the steadiness and evenness of pull, are difficult to reproduce artificially during regeneration. The usual clinical precaution to apply postoperative stretch by small and gentle steps, is well taken. Nevertheless, there is an elasticity and plasticity limit beyond which stretch cannot be carried without serious damage.

In this connection, two points of great practical significance call for attention: the scale on which nerve stretch is to be measured; and the differential effect of stretch on the proximal and distal stumps. As for the former point, it is evident that stretch must be referred to the length of the portion actually undergoing extension. The stress produced by lengthening a five-inch segment by one inch will be twice that of lengthening a ten-inch segment by the same amount. Extensibility of a nerve will, therefore, have to be expressed in percentage of free length, and not in absolute units. If the maximum stretch limit were, say, ten per cent, gradual lengthening by one inch of a stump free to yield over a length of more than ten inches would cause no damage. However, that same one-inch extension would be fatal to another nerve stump that is free for no more than two inches, as this would amount to a fifty per cent extension, which is more than that short nerve piece could stand. In other words, stretch by only a fraction of an inch in one case may impose a much greater strain upon the nerve than stretch of more than one inch in another case.

What length of the nerve is free to yield will often be difficult to ascertain. While liberal mobilization at the time of the operation may free the nerve ends for a sufficient distance up and down, this makes allowance for only such stretch as will be exerted in uniting the ends. All additional stretching, however, to be applied later in the interest of straightening the joints and lengthening the nerve, deals with a wholly unpredictable situation in that adhesions formed in the meantime between the nerve and its bed will have reduced the free portions, which can yield to the stresses, to an unknown fraction of the original length.

The second point to be considered is that a degree of stretch which would rupture the nerve fibers in the proximal stump, might not interfere with nerve regeneration at all when applied to the distal stump. The pathway function of the latter could hardly be assumed to suffer from the rupturing of some neurilemmal tubes and the separation and extension of some Schwann cell columns. The ratio according to which a given amount of stretch will apportion itself between the two stumps will vary with the site of the lesion relative to the moving joint, the fixation of the stumps by adhesions, and the coefficients of extensibility, which will presumably differ for the two stumps. Thus again, each case presents a problem of its own. Moreover, aside from its effects on the nerve fibers, overstretch presents the danger of intraneural hemorrhages from ruptured vessels.

Obviously the technological realities of each case must be duly taken into account. The preceding remarks could no more than briefly expose the situation in its complexity. Continued systematic research would aid materially in removing nerve stretching from the realm of adventure.

The Irreducible Gap. The beneficial effect of a short gap between the nerve ends, discussed earlier, raises the question of the critical length beyond which a gap becomes detrimental to nerve regeneration. This knowledge is indispensable in deciding what to do about gaps that cannot be further reduced by other methods short of grafting. The main factors varying with the length of the gap and the volume of blood which fills it are: degree of syneresis and of the resulting tension; fibrin orientation; intensity of fibrinolysis; rate of vascular penetration; rate and extent of Schwann cell immigration; retention of liquid; collagen deposition; and in further consequence, the rate, orderliness and density of axon passage. With so many variables involved, it is obvious that even the many hundreds of cases of our experience are far from adequate for quantitative evaluation. Any conclusions drawn from them are tentative and subject to future revision.

With this reservation, however, the critical length of the gap can be set at about one to two times the diameter of the nerve. Proportionately longer gaps do not seem to insure optimal conditions for nerve regeneration. This is not to imply that in individual cases much greater distances cannot be successfully spanned, but statistically the prospect of success will decline with the length of the gap. The value just given refers to gaps filled with normal blood. The aspect changes when other fillings are interposed between the nerve stumps. Comparative studies with sleeves filled with Ringer's solution, pure blood plasma, and whole blood of varying composition, have led to the following results.*

Ringer's solution was evidently replaced by a coagulum of nerve exudate and serum. The union tissue forming in this matrix becomes more compact than under standard conditions, and the regenerating nerve fibers have to contend with appreciable fibrosis. This was even more pronounced after the use of pure blood plasma.[200] In this case, syneresis of the clot seems to have been weak, possibly due to the absence of blood platelets, and the orientation of the fibrin pattern, consequently, remained incomplete; above all, the density of the union tissue exceeded by far the range considered favorable for nerve regeneration. Collagen deposition was fairly extensive, and the compactness of the tissue left no adequate liquid spaces for the lateral expansion of regenerated nerve fibers. As a result such unions showed numerous fibrotic foci, with arrested, circling and tortuous nerve fibers, not unlike those seen in ordinary suture scars, though on a smaller scale. There were signs of constriction on many fibers, which implies, as was explained above, impairment of the recovery of fiber caliber. The unfavorable performance of

* Most of these experiments have not been previously published.

blood plasma as a gap filling must evidently be ascribed partly to poor syneresis, but mostly to the fact that it lacks the vast liquefied spaces which develop in whole blood as a result of hemolysis and fibrinolysis.

In an attempt to reduce the consistency of the clot in the gap even below that of whole blood, experiments were undertaken in which fragments of the proteolytic buffy coat (leukocytes) of centrifuged blood were added to whole blood in the splicing sleeve. In these experiments, gaps measuring several centimeters were left between the nerve ends and filled with the modified blood. Three cat nerves so treated gave fair functional regeneration; muscle volume had returned to 71 per cent of normal in one animal which died after $4\frac{1}{2}$ months, an interval too short for full recovery. Histologically, the picture was not nearly as good as with short gaps. The nerve fibers had regenerated in rather tortuous courses, and there was definitely more fibrous tissue between them than is common in ordinary sleeve splicing. This may have been due in part to the measurable constrictions which these long arterial sleeves gradually developed, putting the tissue inside under pressure. Or it may be that blood columns of such length, even with added leukocytes, do not undergo enough liquefaction, hence, become fibrotic. At any rate, these cases demonstrate that fairly satisfactory regeneration can be obtained with gaps as long as twenty times the diameter of the nerve. Nevertheless, the potential dangers of long gaps, particularly in larger nerves, are too great to take the risk clinically as long as other methods, including grafting, can be applied.

Plasma Union. The use of blood plasma for linking ends of severed nerves[64,67,141,163,164,165,207] shares one important feature with sleeve splicing, namely, the omission of sutures near the lesion. In facility of execution, it rates about intermediate between sleeve splicing and ordinary suturing. Satisfactory results have been reported in animals. Judged by the standards outlined previously in this article, plasma suture compares with sleeve splicing about as follows.

Insulation against extraneous tissue is presumably insured by the action of longitudinal traction on the plasma coat. The resulting orientation effect is fully capable of transforming this coat into a firm sheath around the nerve. Orientation inside the union tissue is likely to be less orderly, as has been already indicated earlier in the text. More specifically, the following circumstances would seem to counteract strict longitudinal organization of the union tissue after plasma suture. In cases in which stretch is required to approximate the stumps, the plasma clot is not firm enough to withstand appreciable tension; its holding power is of the same low order as that of sleeves and hence must be supplemented, just as in the case of sleeves, by a remote tension suture. This measure deprives the union tissue of longitudinal traction and leaves syneresis of the clot the sole tension-producing factor. Since experience has shown that the syneretic shrinkage of pure plasma is very slight in comparison to that of whole blood, only negligible tensions will be generated at plasma junctions unless there is a sizable hemorrhage between the stumps.

Moreover, even those tensions that do develop will not have the required pattern. Since the matrix between the nerve stumps, no matter whether it consists of plasma seeping into the crevices or of a hemorrhagic clot, contains fibrin, it will merge with the surface coat into a single mass. The union tissue will therefore fail to undergo the lateral detachment indispensable for longitudinal orientation. Instead, the tensions, and hence, the pathway structure, will assume a pattern radiating in all possible directions. Though a certain amount of self-straightening may occur in the union tissue after it has become repopulated by cells, it is difficult to imagine that even the best plasma junction could ever approach the orderliness of a sleeve junction.

A second and possibly more serious defect of plasma unions is the practically unavoidable seeping of some of the plasma between the cut surfaces of the nerve. The danger inherent in the progressive condensation of this matrix because of lack of fibrinolytic enzymes, lack of liquid spaces for nerve fiber expansion, and heavy collagen deposition, was outlined earlier in this paper. It cannot be repeated too often that compactness of the union tissue is one of the major impediments of nerve regeneration. The observation that nerve fibers regenerate at significantly slower rates after plasma union than after mere crushing,[64,65,67] may be an expression of some defects at the suture line.

For the reasons outlined, plasma suture does not seem to approximate sleeve splicing in performance. It must be stressed, however, that we do not yet know whether or how much practical significance will have to be attached to the features mentioned. It may turn out that their importance would not show up except statistically.

Nerve Wrapping, Tubulization, etc. From the description of the *modus operandi* of sleeve splicing given above, it should have become plain that the resemblance between this method and past practices of nerve wrapping and tubulation (variously called "tubulization" and "tubularization") is only a superficial one. They all have in common the sheathing in of the lesion, but they differ fundamentally in purpose and execution. Consequently, the satisfactory results of sutureless sleeve splicing do not necessarily conflict with the predominantly unfavorable opinions on those other methods, as practised in the past.[22,130,139,155]

The professed purpose of wrapping nerve sutures with membranes of various descriptions has been to prevent penetration of scar tissue and escape of nerve fibers; that of tubulation, to pipe the regenerating fibers from the proximal into the distal stump through extensive gaps. Both methods have failed in principle because they were based on crude and inadequate conceptions of the mechanics of nerve and scar growth. Both proceeded from essentially macroscopic considerations, ignoring the fact that success or failure are decided not in macroscopic dimensions, but on the microscopic and submicroscopic level, where the cells move and operate. We now know that nerve repair cannot be compared to a plumbing job, that a semblance

of mechanical insulation of the suture site is no insurance against cicatrization, and that an empty pipeline is no suitable link over a nerve gap.

The literature on the subject is controversial and often difficult to assess because of lack of rigorous standards in executing and describing the operations, and in rating the results obtained. Table 1 on page 401 lists the principal experimental and clinical reports on the sheathing of nerve stumps, either for insulation or for the bridging of gaps. The list makes no claim to completeness. Moreover, the various entries are of very unequal value; some cover carefully controlled work, others constitute rather casual reports. Purely speculative recommendations or warnings have been omitted. In the following comments the individual articles will be referred to by their order numbers as listed in Table 1.

To consider wrapping measures first, most of them were by their very nature unfit to provide the intended safeguards against cicatrization. Some potentially scar-producing tissue, notably epineurium, remains inside of the wrapping. When the material is used in sheet form (split arteries, fascia, etc.), additional connective tissue can enter through the seam or between the overlapping edges. If the wrapping is loose, it admits further connective tissue from the ends. As was stated above, the presence of such connective tissue need not in itself be harmful to the nerve. If it can be forced into alignment along the outside of the nerve, as it is in sutureless sleeve splicing, it will not interfere with nerve regeneration. However, since in practically all wrapping techniques the nerve ends are first of all sutured, and since the very effect of suturing, for the various reasons outlined above, is to favor ingrowth from the surface into the interior of the nerve, loose wrapping over sutures is of questionable value.

If, on the other hand, one tries to minimize connective-tissue penetration by wrapping the nerve tightly, subsequent contraction of the coat may produce constrictions as serious as those of primary scars (27). Wrappings subject to early erosion and resorption are not only ineffectual but may be harmful by prolonging the proliferative period of the surrounding connective tissue. Unfavorable results must likewise be expected from materials that evoke strong foreign body reactions because of chemical incompatibility with the host tissues, or of liberation of irritating substances, or simply by mechanical irritation (rough surfaces; sharp edges and creases; etc.). However, it cannot be denied that wrapping even over sutures may have some merit if it is done with an elastic, non-constricting, non-irritative, non-porous material resistant to resorption and fragmentation (5, 9, 10, 11, 12, 14, 16, 18, 19, 21, 23, 26, 27, 37, 46, 49, 52).

In contrast, tubulation has met rather generally with clinical failure. Closer inspection of the various procedures that have been tried indicates that the execution rather than the principle was wrong. The ideal substratum for nerve regeneration is degenerated peripheral nerve, and no substitute that would even remotely approach it in adequacy has as yet been discovered. Hence, whatever the medium filling the gap between the nerve stumps

may be, growth in it will be inferior to that in the distal stump or even in a graft. Yet there are different degrees of inferiority, and the better the conditions, the greater will be the length of gap that can be successfully spanned by a sufficient volume of Schwann cells and nerve fibers. For example, good regeneration in arterial sleeves filled with blood with increased fibrinolytic potency was reported above to have occurred over gaps of several centimeters, and there is no reason to question similar reports of earlier authors. But with increasing length of the gap, the hazards to nerve growth increase, and the slightest additional handicap may imperil the whole further progress of regeneration.

The most patent shortcomings were the following:

Open space between the nerve and tube wall. Since it is technically impossible to place cylindrical tubes of wholly or nearly unelastic material over a nerve unless they are wider than the nerve, an open space between sleeve and nerve is almost unavoidable with such materials. Actually, this is the way in which the operation of "tubulization" is usually depicted (Stookey,[155] Fig. 44). Such spaces obviously admit fibrous connective tissue into the gap, preclude the establishment of a longitudinal tension pattern, lead to distortion of the newly forming union tissue and offer an outlet for the indispensable liquid content of the gap.

Perforation and resorption. Tube walls which, even though macroscopically of solid appearance, are full of microscopic pores, are bound to sponge up the regenerating Schwann cells and nerve fibers (28) because of the local suction-like action they exert on the matrix (Fig. 6C). It is immaterial whether these perforations have been present from the beginning or have developed within the first few weeks by erosion. Larger holes act as unfavorably as do the lateral spaces mentioned in the preceding paragraph. Tubes subject to quick resorption (1, 2, 5, 8, 11, 13, 29), or disintegration (6) may, therefore, not only fail to have any beneficial effects, but be actually harmful.

Foreign materials. Tubes from substances foreign and irritative to the body (22, 25, 39, 45, 47, 52) may evoke extensive inflammatory and fibrous reactions, the products of which disrupt the young union tissue and produce heavy scarring in its place.

Collapse. Tubes too flabby to retain their shape collapse and may become completely occluded, thus naturally obstructing nerve regeneration (28, 39, 48).

Inadequate gap fillings. Natural as well as artificial fillings have been used in connection with tubulation, mostly with little knowledge of, and regard for, the requirements of nerve growth. The most spectacular mistake has been the suggestion of Edinger (30) to fill tubes with agar-agar or gelatine, on the supposition that nerves would easily pervade that mass because of its "softness." The method proved a complete failure (34, 35, 36, 39, 40, 41, 42, 44). So did the fantastically unrealistic charging of tubes with dog's fat, fat mixed with lecithin, and brain pulp (39). Of course, no filling that does not afford abundant internal interfaces, such as are formed by the

precipitation of fibers, has any chance of becoming invaded by Schwann cells and axons. Any inert mass that does not have the proper chemical and colloidal properties will become blocked off from the living tissue and serve only as obstruction to growth; while any resorbable mass is apt to become replaced by dense connective tissue. Moreover, not only the original composition of the gap filling, but all its subsequent modifications as well as physical transformations must be taken into consideration. For example, a blood clot can serve as a proper gap filling only if the lysate arising from its liquefaction remains collected. The more this fluid is allowed to become dissipated, the denser and more impervious to cell and axon growth will the matrix become. This finds expression in the common experience that hemorrhage between the nerve ends is followed by fibrosis (26, 28, 39, 48). Such fibrosis could presumably be checked by providing for an adequate degree of enzymatic liquefaction of the clot and by safeguards against loss of the resulting fluid.

Some reports on tubulization speak of the space between the nerve ends as having been left "empty" (34, 35, 38, 44). As explained earlier, this is physically absurd. There must have been either air or saline solution or blood or a serous exudate present at first, but since the subsequent fate of these fortuitous fillings, undergoing absorption, transformation, replacement, etc., has remained unknown, it is impossible to determine just what conditions nerve regeneration had to contend with in these instances.

Constriction. Just as is the case with simple wrappings, tubes that are subject to gradual shrinkage may strangle the covered nerve segment, either during regeneration or later (27). Tubes that provoke heavy scar formation along their outer surface without being able to withstand the constrictive force of this scar, likewise cause strangulation.

Most of the well-intentioned measures listed above have suffered not merely from poor execution, but primarily from lack of a clear conception of how they were to attain their objectives. This is excusable in view of the fact that at the time when they were devised analytical understanding (not to be confounded with histological description) of nerve regeneration was still in a very rudimentary state. It would be less excusable, however, to continue to violate or ignore the rules that in the meantime have been revealed to govern nerve regeneration. It has been the prime purpose of this article to show that these rules cannot be formulated in terms of the macroscopic manipulations of the surgeon, but only in terms of the micromechanics of the nerve fibers, their accessory cells, and their environment. The macroscopic aspect of wrappings, scars, "obstructions," "neuromas" and the like, as such, is irrelevant and often misleading. The microscopic and submicroscopic levels are the domain in which the real mechanisms of nerve repair operate, and it is to those levels that one must look for the decision between success and failure. Devices or manipulations that look quite promising from a purely macroscopic viewpoint, often are revealed by micromechanical analysis to be

wholly absurd; hence, will lead to equally absurd results in practical application.

The only safe guide in the long run would, therefore, seem to be for the surgeon to become so thoroughly familiar with the biology and microtechnology of the tissues concerned with nerve repair that he will automatically come to view his macroscopic manipulations in terms of their micromechanical consequences; that he will cease to think of tubes as pipes, of sheaths as shields, of connective tissue as necessarily obstructive, or of dense vascularization as invariably desirable, and will instead turn his attention to the microstructural frame in which cells and nerve fibers move. He will then learn to calculate the play of tensions, fiber coagula, syneretic and proteolytic changes, and to recognize their sources; to understand the intricate interrelations of Schwann cells, axons, macrophages, and fibroblasts with one another and with their matrix and to let his actions be guided by this insight.

REFERENCES

1. Abercrombie, M., and Johnson, M. L. The outwandering of cells in tissue cultures of nerves undergoing Wallerian degeneration. *J. exp. Biol.*, 1942, *19:* 266–283.
2. Adams, W. E. The blood supply of nerves. I. Historical review. *J. Anat., Lond.*, 1942, *76:* 323–341.
3. Adams, W. E. The blood supply of nerves. II. The effects of exclusion of its regional sources of supply on the sciatic nerve of the rabbit. *J. Anat., Lond.*, 1943, *77:* 243–250.
4. Aird, R. B., and Naffziger, H. C. Regeneration of nerves after anastomosis of small proximal to larger peripheral nerves. An experimental study concerned with relief of peripheral neurogenic paresis. *Arch. Surg., Chicago*, 1939, *38:* 906–916.
5. Auerbach, S. Galalith zur Tubulisation der Nerven nach Neurolysen und Nervennähten. *Münch. med. Wschr.*, 1915, *62:* 1457–1458.
6. Auerbach, S. Zur Frage der Nerveneinscheidung mittelst Galalith. *Münch. med. Wschr.*, 1916, *63:* 1573–1574.
7. v. Auffenberg, F. Ueber Nervennaht und -lösung. *Arch. klin. Chir.*, 1907, *82:* 615–657.
8. Babcock, W. W. A standard technique for operations on peripheral nerves. With especial reference to the closure of large gaps. *Surg. Gynec. Obstet.*, 1927, *45:* 364–378.
9. Baitsell, G. A. A study of the clotting of the plasma of frog's blood and the transformation of the clot into a fibrous tissue. *Amer. J. Physiol.*, 1917, *44:* 109–131.
10. Barron, D. H. Central course of "recurrent" sensory discharges. *J. Neurophysiol.*, 1940, *3:* 403–406.
11. Bentley, F. H., and Hill, M. Nerve grafting. *Brit. J. Surg.*, 1936, *24:* 368–387.
12. Bentley, F. H., and Schlapp, W. Experiments on the blood supply of nerves. *J. Physiol.*, 1943, *102:* 62–71.
13. Berry, C. M., Grundfest, H., and Hinsey, J. C. The electrical activity of regenerating nerves in the cat. *J. Neurophysiol.*, 1944, *7:* 103–115.
14. Bethe, A. Neue Versuche über die Regeneration der Nervenfasern. *Pflüg. Arch. ges. Physiol.*, 1907, *116:* 385–478.
15. Bethe, A. Notiz über die Unfähigkeit motorischer Fasern mit rezeptorischen Fasern zu verheilen. *Pflüg. Arch. ges. Physiol.*, 1907, *116:* 479–481.
16. Bethe, A. Zwei neue Methoden der Ueberbrückung grösserer Nervenlücken. *Dtsch. med. Wschr.*, 1916, *2:* 1311–1314.
17. Bielschowsky, M., and Unger, E. Die Überbrückung grosser Nervenlücken. Beiträge zur Kenntnis der Degeneration und Regeneration peripherischer Nerven. *J. Psychol. Neurol., Lpz.*, 1918, *22:* 267–318.
18. Billig, H. E. and van Harreveld, A. A new aspect of muscle reinnervation. *Nav. med. Bull., Wash.*, 1943, *41:* 410–414.
19. Blencke, A. Ein weiterer Beitrag zu den Ueberbrückungsversuchen von Nervendefekten mit Edinger-Röhrchen. *Zbl. Chir.*, 1917, *44:* 236–238.

20. Boeke, J. Studien zur Nervenregeneration II. Die Regeneration nach Vereinigung ungleichartiger Nervenstücke (heretogene Regeneration), und die Funktion der Augenmuskel- und Zungennerven. Die allgemeinen Gesetze der Nervenregeneration. *Verh. Akad. Wet., Amst.*, 1917, *19:* no. 5, 1–71.
21. Boeke, J. Nervenregeneration. *Bumke u. Foersters Handb. Neurol.*, 1935, *1:* 995–1122.
22. Bristow, R. Discussion on injuries to peripheral nerves. *Proc. R. Soc. Med.*, 1941, *34:* 513–517.
23. v. Büngner, O. Ueber die Degenerations- und Regenerationsvorgänge am Nerven nach Verletzungen. *Beitr. path. Anat.*, 1891, *10:* 321–393.
24. Burk, W. Zu den Ueberbrückungsversuchen von Nervendefekten. (Bemerkungen zu der gleichlautenden Arbeit von Stracker. Zentralblatt für Chirurgie Nr. 50. 1916.) *Zbl. Chir.*, 1917, *44:* 238.
25. Burke, G. L. The corrosion of metals in tissues; and an introduction to tantalum. *Canad. med. Ass. J.*, 1940, *43:* 125–128.
26. Burr, H. S. An electro-dynamic theory of development suggested by studies of proliferation rates in the brain of Amblystoma. *J. comp. Neurol.*, 1932, *56:* 347–371.
27. Burt, A. S. Chemical factors in nerve growth studied in tissue culture: Vitamin B_1 and the growth of spinal ganglia. *J. cell. comp. Physiol.*, 1943, *21:* 145–159.
28. Burt, A. S. Growth of spinal ganglia in plasma from vitamin B_1-deficient chickens. *J. cell. comp. Physiol.*, 1943, *22:* 205–222.
29. Burt, A. S. Effect of biotin on chick spinal ganglia in tissue culture. *Proc. Soc. exp. Biol., N. Y.*, 1943, *54:* 191–193.
30. Cajal, S. Ramon y La rétine des vertébrés. *Cellule*, 1893, *9:* 119–255.
31. Cajal, S. Ramon y Degeneration and regeneration of the nervous system. *London: Oxford Univ. Press*, 1928, 2 vols.
32. Child, C. M. The origin and development of the nervous system, from a physiological viewpoint. *Chicago: Univ. of Chicago Press*, 1921, 296 pp.
33. Coleman, C. C. Surgical treatment of peripheral nerve injuries. *Surg. Gynec. Obstet.*, 1944, *78:* 113–124.
34. Craig, A. B., and Ellis, A. G. An experimental and histological study of Cargile membrane. With reference to (1) its efficacy in preventing adhesions in the abdominal and cranial cavities and around nerves and tendons, and (2) its ultimate fate in the tissues. *Ann. Surg.*, 1905, *41:* 801–822.
35. Davenport, H. A., Chor, H., and Dolkart, R. E. The ratio of myelinated to unmyelinated fibers in regenerated sciatic nerves of Macacus rhesus. *J. comp. Neurol.*, 1937, *67:* 483–491.
36. Davis, L., and Cleveland, D. A. Experimental studies in nerve transplants. *Ann. Surg.*, 1934, *99:* 271–283.
37. Denk, W. Ueber Schussverletzungen der Nerven. *Beitr. klin. Chir.*, 1914, *91:* 217–221.
38. Detwiler, S. R. Neuroembryology. An experimental study. *New York: The Macmillan Co.*, 1936, 218 pp.
39. Dogliotti, A. M. Études expérimentales et première application clinique d'une nouvelle opération destinée à augmenter et à équilibrer la fonction neuro-musculaire dans la paralysie partielle des nerfs. *J. Chir., Paris*, 1935, *45:* 30–48.
40. Dustin, A. P. Le rôle des tropismes et de l'odogenèse dans la régénération du système nerveux. *Arch. Biol., Paris*, 1910, *25:* 269–388.
41. Dustin, A. P. Les lésions posttraumatiques des nerfs. Contribution à l'histopathologie du système nerveux périphérique chez l'homme. *Ambulance de l'Ocean, Paris*, 1917, *1:* fasc. 2, 71–161.
42. v. Ebner, V. Über die Entwicklung der leimgebenden Fibrillen, besonders im Zahnbein. *S.B. Akad. Wiss. Wien*, 1906, *115:* 281–343.
43. Eden, R. Sind zur Ueberbrückung von Nervendefekten die Verfahren der Tubulisation und der Nerventransplantation zu empfehlen? *Zbl. Chir.*, 1917, *44:* 138–140.
44. Eden, R., and Rehn, E. Die autoplastische Fetttransplantation zur Neurolysis und Tendolysis. (Klinik und Experiment.) *Arch. klin. Chir.*, 1914, *104:* 65–83.
45. Edinger, L. Ueber die Vereinigung getrennter Nerven. Grundsätzliches und Mitteilung eines neuen Verfahrens. *Münch. med. Wschr.*, 1916, *63:* 225–228.
46. Elsberg, C. A. Experiments on motor nerve regeneration and the direct neurotization of paralyzed muscles by their own and by foreign nerves. *Science*, 1917, *45:* 318–320.
47. v. Enderlen and Lobenhoffer. Zur Ueberbrückung von Nervendefekten. *Münch. med. Wschr.*, 1917, *64:* 225.
48. Erlacher, P. Experimentelle Untersuchungen über Plastik und Transplantation von Nerv und Muskel. *Arch. klin. Chir.*, 1914, *106:* 389–407.
49. Erlanger, J. and Gasser, H. S. Electrical signs of nervous activity. *Philadelphia: Univ. of Pennsylvania Press*, 1937, 221 pp.

50. Fischer, E. Yeast, thiamin and biotin on atrophy and regeneration of denervated skeletal muscle. *Fed. Proc. Amer. Soc. exp. Biol.*, 1943, *2:* 13.
51. Foramitti, C. Zur Technik der Nervennaht. *Arch. klin. Chir.*, 1904, *73:* 643–648.
52. Ford, F. R., and Woodhall, B. Phenomena due to misdirection of regenerating fibers of cranial, spinal and autonomic nerves. Clinical observations. *Arch. Surg., Chicago*, 1938, *36:* 480–496.
53. Forssman, J. Ueber die Ursachen, welche die Wachsthumsrichtung der peripheren Nervenfasern bei der Regeneration bestimmen. *Beitr. path. Anat.*, 1898, *24:* 56–100.
54. Forssman, J. Zur Kenntniss des Neurotropismus. Weitere Beiträge. *Beitr. path. Anat.*, 1900, *27:* 407–430.
55. Fort, W. B. An experimental study of the factors involved in the establishment of neuromuscular connections. (Thesis) *Univ. Chicago*, 1940, 88 pp.
56. Frey-Wyssling, A. Submikroskopische Morphologie des Protoplasmas und seiner Derivate. *Berlin: Gebrüder Borntraeger*, 1938, xv: 317 pp.
57. Fullerton, A. On the use of a sleeve of vein in nerve suture. *Brit. med. J.*, 1915, *2:* 320.
58. Gluck, T. Ueber Neuroplastik auf dem Wege der Transplantation. *Arch. klin. Chir.*, 1880, *25:* 606–616.
59. Gosset, A., and Bertrand, I. La moelle épinière, utilisée comme greffon hétéroplastique dans les blessures des nerfs périphériques. Recherches cliniques et expérimentales. *J. Chir., Paris*, 1938, *51:* 481–505.
60. Gray, P. Experiments with direct currents on chick embryos. *Arch. EntwMech. Org.*, 1939, *139:* 732–779.
61. Greenfield, J. G. Recent studies of the morphology of the neurone in health and disease. *J. Neurol. Psychiat.*, 1938, n.s. *1:* 306–328.
62. Greenfield, J. G. Discussion on injuries to peripheral nerves. *Proc. R. Soc. Med.*, 1941, *34:* 519.
63. Greenman, M. J. Studies on the regeneration of the peroneal nerve of the albino rat: Number and sectional areas of fibers: Area relation of axis to sheath. *J. comp. Neurol.*, 1913, *23:* 479–513.
64. Gutmann, E. Factors affecting recovery of motor function after nerve lesions. *J. Neurol. Psychiat.*, 1942, n.s. *5:* 81–95.
65. Gutmann, E., Guttmann, L., Medawar, P. B., and Young, J. Z. The rate of regeneration of nerve. *J. exp. Biol.*, 1942, *19:* 14–44.
66. Gutmann, E., and Guttmann, L. Factors affecting recovery of sensory function after nerve lesions. *J. Neurol. Psychiat.*, 1942, n.s. *5:* 117–129.
67. Gutmann, E., and Sanders, F. K. Recovery of fibre numbers and diameters in the regeneration of peripheral nerves. *J. Physiol.*, 1943, *101:* 489–518.
68. Hamilton, H. L., and Plotz, H. Use of biotin for stimulating growth of nerve tissue and other cells *in vitro*. *Proc. Soc. exp. Biol., N. Y.*, 1942, *50:* 133–135.
69. Hammond, W. S., Nonidez, J. F., and Hinsey, J. C. Effect of various sulfonamide compounds on nerve regeneration. *Arch. Neurol. Psychiat., Chicago*, 1943, *50:* 499–509.
70. Hans, H. Naht durchtrennter Nerven mittels Einhülsung in Eigengewebe. *Zbl. Chir.*, 1915, *42:* 801–802.
71. Harrison, R. G. The outgrowth of the nerve fiber as a mode of protoplasmic movement. *J. exp. Zool.*, 1910, *9:* 787–848.
72. Harrison, R. G. The cultivation of tissues in extraneous media as a method of morphogenetic study. *Anat. Rec.*, 1912, *6:* 181–193.
73. Harrison, R. G. The reaction of embryonic cells to solid structures. *J. exp. Zool.*, 1914, *17:* 521–544.
74. Harrison, R. G. The Croonian lecture. On the origin and development of the nervous system studied by the methods of experimental embryology. *Proc. roy. Soc., Lond.*, 1935, *118B:* 155–196.
75. Hashimoto, T., and Tokuoka, H. Ueber die Schussverletzungen peripherer Nerven und ihre Behandlung (Tubulisation). *Arch. klin. Chir.*, 1907, *84:* 354–402.
76. Heile, B., and Hezel, O. Unsere bisherigen Erfahrungen bei der Behandlung im Kriege verletzter peripherer Nerven. *Beitr. klin. Chir.*, 1915, *96:* 299–328.
77. Held, H. Die Entwickelung des Nervengewebes bei den Wirbeltieren. *Leipzig: J. A. Barth*, 1909, 378 pp.
78. Highet, W. B., and Sanders, F. K. The effects of stretching nerves after suture. *Brit. J. Surg.*, 1943, *30:* 355–369.
79. Hirschel, G. Erfahrungen über Schussverletzungen der Nerven und die Verwendung von präparierten Kalbsarterien zu ihrer Umhüllung. *Dtsch. Z. Chir.*, 1915, *132:* 567–573.
80. His, W. Die Entwickelung der ersten Nervenbahnen beim menschlichen Embryo. Uebersichtliche Darstellung. *Arch. Anat. Physiol., Lpz.* 1887, 368–378.

81. Hohmann, G., and Spielmeyer, W. Zur Kritik des Edingerschen und des Betheschen Verfahrens der Ueberbrückung grösserer Nervenlücken. *Münch. med. Wschr.*, 1917, *64:* 97–99.
82. Holmes, W., and Young, J. Z. Nerve regeneration after immediate and delayed suture. *J. Anat., Lond.*, 1942, *77:* 63–96.
83. Holobut, W. S., and Jalowy, B. Die De- und Regeneration des peripheren motorischen Nervensystems auf einer morphologischfunktionellen Grundlage. *Z. Zellforsch.*, 1936, *25:* 541–564.
84. Howell, W. H., and Huber, G. C. A physiological, histological and clinical study of the degeneration and regeneration in peripheral nerve fibres after severance of their connections with the nerve centres. *J. Physiol.*, 1892, *13:* 335–406.
85. Huber, G. C. A study of the operative treatment for loss of nerve substance in peripheral nerves. *J. Morph.*, 1895, *11:* 629–740.
86. Huber, G. C. Transplantation of peripheral nerves. *Arch. Neurol. Psychiat., Chicago*, 1919, *2:* 466–480.
87. Huber, G. C. Repair of peripheral nerve injuries. *Surg. Gynec. Obstet.*, 1920, *30:* 464–471.
88. Huber, G. C. Nerve degeneration and regeneration. In: Stookey, B. *Surgical and mechanical treatment of peripheral nerves.* Philadelphia: W. B. Saunders Co., 1922, 41–79.
89. Huber, G. C. Experimental observations on peripheral nerve repair. In: *The Medical Department of the United States Army in the World War.* Washington: Govt. Printing Office, 1927, *11:* 1091–1283.
90. Ingebrigtsen, R. Studies of the degeneration and regeneration of axis cylinders in vitro. *J. exp. Med.*, 1913, *17:* 182–191.
91. Ingebrigtsen, R. A contribution to the biology of peripheral nerves in transplantation. II. Life of peripheral nerves of mammals in plasma. *J. exp. Med.*, 1916, *23:* 251–264.
92. Ingvar, S. Reactions of cells to the galvanic current in tissue cultures. *Proc. Soc. exp. Biol., N. Y.*, 1920, *17:* 198–199.
93. Kappers, C. U. A. Further contributions on neurobiotaxis: IX. An attempt to compare the phenomena of neurobiotaxis with other phenomena of taxis and tropism. The dynamic polarization of the neurone. *J. comp. Neurol.*, 1917, *27:* 261–298.
94. Karssen, A., and Sager, B. Sur l'influence du courant électrique sur la croissance des neuroblastes in vitro. *Arch. exp. Zellforsch.*, 1934, *16:* 255–259.
95. Kirk, E. G., and Lewis, D. D. Fascial tubulization in the repair of nerve defects. *J. Amer. med. Ass.*, 1915, *65:* 486–492.
96. Kirk, E. G., and Lewis, D. D. Regeneration in peripheral nerves. An experimental study. *Johns Hopk. Hosp. Bull.*, 1917, *28:* 71–80.
97. Kirschner, M. Zur Behandlung grosser Nervendefekte. *Dtsch. med. Wschr.*, 1917, *43:* 739–741.
98. Kölliker, T. Die Verletzungen und chirurgischen Erkrankungen der peripherischen Nerven. *Dtsch. Chir. Lief. 24b. Stuttgart: F. Enke*, 1890, 120 pp.
99. Kraus, H., and Reisner, H. Behandlungsergebnisse von Verletzungen peripherer Nerven mit besonderer Berücksichtigung der Schussverletzungen der Jahre 1919, 1927 und 1934. *Arch. klin. Chir.*, 1940, *199:* 318–336.
100. Kredel, L. Ueber das Verhalten der auf operierte schussverletzte Nerven überpflanzten Fascienlappen. *Zbl. Chir.*, 1915, *42:* 201–203.
101. Lazere, B., Thomson, J. D., and Hines, H. M. Studies on muscle and nerve in biotin-deficient rats. *Proc. Soc. exp. Biol., N. Y.*, 1943, *53:* 81–82.
102. Levi, G. Explantation, besonders die Struktur und die biologischen Eigenschaften der in vitro gezüchteten Zellen und Gewebe. *Ergebn. Anat. EntwGesch.*, 1934, *31:* 125–707.
103. Litwiller, R. Quantitative studies on nerve regeneration in amphibia. I. Factors controlling nerve regeneration in adult limbs. *J. comp. Neurol.*, 1938, *69:* 427–447.
104. Lloyd, D. P. C. Centripetal discharges in dorsal and ventral roots following stimulation of muscle by ventral root volleys. *Proc. Soc. exp. Biol., N. Y.*, 1941, *47:* 44–47.
105. Lloyd, D. P. C. Stimulation of peripheral nerve terminations by active muscle. *J. Neurophysiol.*, 1942, *5:* 153–165.
106. Lotheissen, G. Zur Technik der Nerven- und Sehnennaht. *Arch. klin. Chir.*, 1901, *64:* 310–313.
107. Lugaro, E. Sul neurotropismo e sui trapianti dei nervi. *Riv. Patol. nerv. ment.*, 1906, *11:* 320–327.
108. McCarrison, R., and Sankaran, G. Effect of plasma from a case of *polyneuritis gallinarum* on growth of tissues *in vitro*. Preliminary note. *Indian J. med. Res.*, 1933, *21:* 187–188.
109. Masson, P. Experimental and spontaneous schwannomas (peripheral gliomas). *Amer. J. Path.* 1932, *8:* 367–416.
110. Mauclaire, P. Suture nerveuse tubulaire avec des trachées de petits animaux. *Bull. Soc. Chir., Paris*, 1915, n.s. *41:* 2402–2404.
111. Meisel, K. Verletzungen peripherer Nerven. *Beitr. klin. Chir.*, 1916, *98:* 758.

112. Meuriot, H., and Platon. Cent observations d'isolement des nerfs par manchonnage au caoutchouc. *Bull. Soc. Chir., Paris*, 1918, *44:* 850–854.
113. Mitchell, S. W. Injuries of nerves and their consequences. *Philadelphia: J. B. Lippincott &Co.*, 1872, 377 pp.
114. Mossa, S. La struttura del citoplasma degli elementi viventi coltivati in vitro studiata alla osservazione in campo oscuro. *Arch. exp. Zellforsch.*, 1927, *4:* 447–461.
115. Müller, O., and Berblinger, W. Das Endergebnis einer nach der Edinger'schen Methode (Agarröhrchen) vorgenommenen Ueberbrückung des Nervus ulnaris mit anatomischer Untersuchung. *Berl. klin. Wschr.*, 1917, *54:* 1109–1111.
116. Naffziger, H. C. Methods to secure end-to-end suture of peripheral nerves. *Surg. Gynec. Obstet.*, 1921, *32:* 193–204.
117. Nageotte, J. Le processus de la cicatrisation des nerfs. *C. R. Soc. Biol., Paris*, 1915, *78:* 249–254.
118. Nageotte, J. Action à distance exercée par les macrophages sur le développement des travées névrogliques et sur la myélinisation des neurites dans les cicatrices nerveuses. *C. R. Soc. Biol., Paris*, 1915, *78:* 711–714.
119. Nageotte, J. L'organisation de la matière dans ses rapports avec la vie. *Paris: Librairie Félix Alcan*, 1922, vi: 560 pp.
120. Nageotte, J. Sheaths of the peripheral nerves. Nerve degeneration and regeneration. In: *Cytology and cellular pathology of the nervous system.* W. Penfield, Ed. New York: P. B. Hoeber, 1932, i: 189–239.
121. Nageotte, J., and Guyon, L. Différences physiologiques entre la névroglie des fibres motrices et celle des fibres sensitives, dans les nerfs périphériques, mises en évidence par la régénération. *C. R. Soc. Biol., Paris*, 1918, *81:* 571–574.
122. Needham, J. Biochemistry and Morphogenesis. *Cambridge: Univ. Press*, 1942, 787 pp.
123. Parker, G. H., and Paine, V. L. Progressive nerve degeneration and its rate in the lateral-line nerve of the catfish. *Amer. J. Anat.*, 1934, *54:* 1–25.
124. Payr, E. Beiträge zur Technik der Blutgefäss- und Nervennaht nebst Mittheilungen über die Verwendung eines resorbirbaren Metalles in der Chirurgie. *Arch. klin. Chir.*, 1900, *62:* 67–93.
125. Perekropoff, A. I. Regeneration of defects of nerve trunks by joining the ends with vascular tubules (arteries and veins). Experimental investigation. (Russian) *Kazan:* 1913, 144 pp.
126. Perthes, G. Die Schussverletzungen der peripheren Nerven. *Z. ges. Neurol. Psychiat.*, 1917, *36:* 400–420.
127. Péterfi, T., and Kapel, O. Die Wirkung des Anstechens auf das Protoplasma der in vitro gezüchteten Gewebezellen. III. Anstichversuche an den Nervenzellen. *Arch. exp. Zellforsch.*, 1928, *5:* 341–348.
128. Picken, L. E. R. The fine structure of biological systems. *Biol. Rev.*, 1940, *15:* 133–167.
129. Platt, H. On the results of bridging gaps in injured nerve trunks by autogenous fascial tubulization and autogenous nerve grafts. *Brit. J. Surg.*, 1919, *7:* 384–389.
130. Pollock, L. J., and Davis, L. Peripheral nerve injuries. *New York: P. B. Hoeber*, 1933, 678 pp.
131. Pomerancew. Zur Casuistik der Nervennaht. (Russian) *Wratsch.*, 1900, no. 1, p. 26.
132. Pudenz, R. H., and Odom, G. L. Meningocerebral adhesions. An experimental study of the effect of human amniotic membrane, amnioplastin, beef allantoic membrane, Cargile membrane, tantalum foil, and polyvinyl alcohol films. *Surgery*, 1942, *12:* 318–344.
133. Ranson, S. W. Degeneration and regeneration of nerve fibers. *J. comp. Neurol.*, 1912, *22:* 487–545.
134. Rexed, B., and Swensson, A. Über die Regeneration der Markscheide bei peripheren Nerven nach Kontinuitätstrennungen. *Z. mikr.-anat. Forsch.*, 1940, *49:* 359–387.
135. Röpke, W. Chirurgische Behandlung der Verletzungen und Erkrankungen der peripheren Nerven. *Penzoldt u. Stintzings Handb. ges. Therapie, Jena*, 1917, *4:* 513–541.
136. Rosenblueth, A., and del Pozo, E. C. The centrifugal course of Wallerian degeneration. *Amer. J. Physiol.*, 1943, *139:* 247–254.
137. Rossi, O., and Gastaldi, G. La rigenerazione del tessuto nervoso nei vertebrati superiori. Rivista critica con dati personali. *Riv. Patol nerv. ment.*, 1935, *46:* 1–369.
138. Saito, M. Zur Frage der Regeneration der peripheren Nerven des erwachsenen Menschen. *Arb. neurol. Inst. (Inst. Anat. Physiol. ZentNerv.) Univ. Wien.*, 1922, *24:* 85–92.
139. Sanders, F. K. The repair of large gaps in the peripheral nerves. *Brain*, 1942, *65:* 281–337.
140. Sanders, F. K., and Young, J. Z. The degeneration and re-innervation of grafted nerves. *J. Anat., Lond.*, 1942, *76:* 143–166.
141. Seddon, H. J., and Medawar, P. B. Fibrin suture of human nerves. *Lancet*, 1942, *2:* 87–88.
142. Sherren, J. Some points in the surgery of the peripheral nerves. *Edinb. med. J.*, 1906, n.s. *20:* 297–332.

143. Speidel, C. C. Studies of living nerves. I. The movements of individual sheath cells and nerve sprouts correlated with the process of myelin-sheath formation in amphibian larvae. *J. exp. Zool.*, 1932, *61:* 279–331.
144. Speidel, C. C. Studies of living nerves. II. Activities of ameboid growth cones, sheath cells, and myelin segments, as revealed by prolonged observation of individual nerve fibers in frog tadpoles. *Amer. J. Anat.*, 1933, *52:* 1–79.
145. Speidel, C. C. Studies of living nerves. III. Phenomena of nerve irritation and recovery, degeneration and repair. *J. comp. Neurol.*, 1935, *61:* 1–78.
146. Speidel, C. C. Studies of living nerves. IV. Growth, regeneration, and myelination of peripheral nerves in salamanders. *Biol. Bull. Wood's Hole*, 1935, *68:* 140–161.
147. Speidel, C. C. Studies of living nerves. VII. Growth adjustments of cutaneous terminal arborizations. *J. comp. Neurol.*, 1942, *76:* 57–73.
148. Sperry, R. W. The effect of crossing nerves to antagonistic muscles in the hind limb of the rat. *J. comp. Neurol.*, 1941, *75:* 1–19.
149. Sperry, R. W. Functional results of crossing sensory nerves in the rat. *J. comp. Neurol.*, 1943, *78:* 59–90.
150. Spielmeyer, W. Histopathologie des Nervensystems. *Berlin: J. Springer*, 1922, vi: 493 pp.
151. Spitzy, H. Bemerkung zur Ueberbrückung von Nervendefekten. *Münch. med. Wschr.*, 1917, *64:* 372.
152. Spurling, R. G. The use of tantalum wire and foil in the repair of peripheral nerves. *Surg. Clin. N. Amer.*, 1943, *23:* 1491–1504.
153. Steinthal, C. Die Deckung grösserer Nervendefekte durch Tubularnaht. *Beitr. klin. Chir.*, 1915, *96:* 295–298.
154. Steinthal, C. Die Ueberdeckung von grösseren Nervendefekten mittels Tubularnaht. *Zbl. Chir.*, 1917, *44:* 646–647.
155. Stookey, B. Surgical and mechanical treatment of peripheral nerves. *Philadelphia: W. B. Saunders Co.*, 1922, 475 pp.
156. Stopford, J. S. B. The treatment of large defects in peripheral nerve injuries. *Lancet*, 1920, *2:* 1296–1297.
157. Stracker, O. Zu den Ueberbrückungsversuchen von Nervendefekten. *Zbl. Chir.*, 1916, *43:* 985–990.
158. Strasser, H. Alte und neue Probleme der entwickelungsgeschichtlichen Forschung auf dem Gebiete des Nervensystems. *Ergebn. Anat. EntwGesch.*, 1891, *1:* 721–769.
159. Stroebe, H. Experimentelle Untersuchungen über Degeneration und Regeneration peripherer Nerven nach Verletzungen. *Beitr. path. Anat.*, 1893, *13:* 160–278.
160. Swan, J. Discussion on injuries to the peripheral nerves. *Proc. R. Soc. Med.*, 1941, *34:* 521–529.
161. Takimoto, G. Ueber die Nervendehnung. Experimentelle und klinische Untersuchung. *Mitt. med. Fak. Tokio*, 1916, *16:* 73–136.
162. Tangari, C. Ricerche sperimentali sull'azione dell'aneurina nei processi rigenerativi del tessuto nervoso periferico. *Arch. Sci. med.*, 1940, *69:* 331–345.
163. Tarlov, I. M., and Benjamin, B. Autologous plasma clot suture of nerves. *Science*, 1942, *95:* 258.
164. Tarlov, I. M., Denslow, C., Swarz, S., and Pineles, D. Plasma clot suture of nerves. Experimental technic. *Arch. Surg., Chicago*, 1943, *47:* 44–58.
165. Tarlov, I. M. Plasma clot suture of nerves. *J. Neurosurg.*, 1944, *1:* 359.
166. Taylor, A. C. Selectivity of nerve fibers from the dorsal and ventral roots in the development of the frog limb. *J. exp. Zool.*, 1944, *96:* 159–185.
167. Tello, F. Gegenwärtige Anschauungen über den Neurotropismus. *Vortr. EntwMech. Org.*, 1923, *33:* 1–73.
168. Tillmanns, H. In: *Chirurgie des praktischen Arztes mit Einschluss der Augen-, Ohren- und Zahnkrankheiten.* W. Ebstein and J. Schwalbe, Ed. Stuttgart: F. Enke, 1907, 944 pp.
169. Treutlein, A. Kriegschirurgisches aus Japan. *Münch. med. Wschr.*, 1906, *53:* 1199–1202.
170. Vanlair, C. De la régénération des nerfs périphériques par le procédé de la suture tubulaire. *Arch. Biol., Paris*, 1882, *3:* 379–496.
171. Vanlair, C. Nouvelles recherches expérimentales sur la régénération des nerfs. *Arch. Biol., Paris*, 1885, *6:* 127–235.
172. Verne, J., and Iselin, M. Réflexions sur deux pièces de réparation nerveuse sur l'homme prélevées dix semaines et six mois après l'opération. *Pr. méd.*, 1941, *49:* 789–791.

173. VULPIUS, O., and STOFFEL, A. Orthopädische Operationslehre. *Stuttgart: F. Enke*, 1920, xvi: 744 pp.
174. WARD, A. A., and KENNARD, M. A. Effect of cholinergic drugs on recovery of function following lesions of the central nervous system in monkeys. *Yale J. Biol. Med.*, 1942, *15:* 189–228.
175. WEDDELL, G., and GLEES, P. The early stages in the degeneration of cutaneous nerve fibres. *J. Anat., Lond.*, 1942, *76:* 65–93.
176. WEISS, P. Functional adaptation and the role of ground substances in development. *Amer. Nat.*, 1933, *67:* 322–340.
177. WEISS, P. In vitro experiments on the factors determining the course of the outgrowing nerve fiber. *J. exp. Zool.*, 1934, *68:* 393–448.
178. WEISS, P. Motor effects of sensory nerves experimentally connected with muscles. *Anat. Rec.*, 1934, *60:* 437–448.
179. WEISS, P. Experimental innervation of muscles by the central ends of afferent nerves (establishment of a one-neurone connection between receptor and effector organ), with functional tests. *J. comp. Neurol.*, 1935, *61:* 135–174.
180. WEISS, P. Selectivity controlling the central-peripheral relations in the nervous system. *Biol. Rev.*, 1936, *11:* 494–531.
181. WEISS, P. Further experimental investigations on the phenomenon of homologous response in transplanted amphibian limbs. II. Nerve regeneration and the innervation of transplanted limbs. *J. comp. Neurol.*, 1937, *66:* 481–535.
182. WEISS, P. Principles of development. A text in experimental embryology. *New York: Henry Holt*, 1939, xix, 601 pp.
183. WEISS, P. Reunion of stumps of small nerves by tubulation instead of suture. *Science*, 1941, *93:* 67–68.
184. WEISS, P. Self-differentiation of the basic patterns of coordination. *Comp. Psychol. Monogr.*, 1941, *17:* no. 4, 96 pp.
185. WEISS, P. Nerve patterns: The mechanics of nerve growth. *Growth*, 1941, *5* (suppl.): 163–203.
186. WEISS, P. Nerve regeneration in the rat following tubular splicing of severed nerves. *Arch. Surg., Chicago*, 1943, *46:* 525–547.
187. WEISS, P. Endoneurial edema in constricted nerve. *Anat. Rec.*, 1943, *86:* 491–522.
188. WEISS, P. Experiments on nerve repair. *Trans. Amer. neurol. Ass. 1943*, 42–45.
189. WEISS, P. Nerve reunion with sleeves of frozen-dried artery in rabbits, cats and monkeys. *Proc. Soc. exp. Biol., N. Y.*, 1943, *54:* 274–277.
190. WEISS, P. Functional nerve regeneration through frozen-dried nerve grafts in cats and monkeys. *Proc. Soc. exp. Biol., N. Y.*, 1943, *54:* 277–279.
191. WEISS, P. In vitro transformation of spindle cells of neural origin into macrophages. *Anat. Rec.*, 1944, *88:* 205–221.
192. WEISS, P. Damming of axoplasm in constricted nerve: a sign of perpetual growth in nerve fibers. *Anat. Rec.*, 1944, *88:* 464.
193. WEISS, P. Sutureless reunion of severed nerves with elastic cuffs of tantalum. *J. Neurosurg.*, 1944, *1:* 219–225.
194. WEISS, P., and BURT, A. S. Effect of nerve compression on Wallerian degeneration *in vitro*. *Proc. Soc. exp. Biol., N. Y.*, 1944, *55:* 109–112.
195. WEISS, P., and CAMPBELL, C. J. Nerve fiber counts and muscle tension after nerve regeneration in the rat. *Amer. J. Physiol.*, 1944, *140:* 616–626.
196. WEISS, P., and CUMMINGS, J. B. Regeneration of the lateral line nerve of Amblystoma from different nerve fiber sources. *Anat. Rec.*, 1943, *87:* 119–125.
197. WEISS, P., and DAVIS, H. Pressure block in nerves provided with arterial sleeves. *J. Neurophysiol.*, 1943, *6:* 269–286.
198. WEISS, P., and LITWILLER, R. Quantitative studies on nerve regeneration in amphibia. I. Factors controlling nerve regeneration in adult limbs. *Proc. Soc. exp. Biol., N. Y.*, 1937, *36:* 636–638.
199. WEISS, P., and TAYLOR, A. C. Repair of peripheral nerves by grafts of frozen-dried nerve. *Proc. Soc. exp. Biol., N. Y.*, 1943, *52:* 326–328.
200. WEISS, P., and TAYLOR, A. C. Histomechanical analysis of nerve reunion in the rat after tubular splicing. *Arch. Surg., Chicago*, 1943, *47:* 419–447.
201. WEISS, P., and TAYLOR, A. C. Further experimental evidence against "neurotropism" in nerve regeneration. *J. exp. Zool.*, 1944, *95:* 233–257.

202. Weiss, P., and Taylor, A. C. Impairment of growth and myelinization in regenerating nerve fibers subject to constriction. *Proc. Soc. exp. Biol., N. Y.*, 1944, *55:* 77–80.
203. Williams, S. C. A study of the reactions of growing embryonic nerve fibers to the passage of direct electric current through the surrounding medium. *Anat. Rec.*, 1936, *64* (suppl. 3): 56–57.
204. Wrede, L. Ueberbrückung eines Nervendefektes mittels Seidennaht und lebenden Venenstückes. *Dtsch. med. Wschr.*, 1909, *35:* 1125.
205. Young, J. Z. The functional repair of nervous tissue. *Physiol. Rev.*, 1942, *22:* 318–374.
206. Young, J. Z. The process of regeneration of nerve and muscle following immediate and delayed suture. *Trans. Amer. neurol. Ass.*, 1943, 41–42.
207. Young, J. Z., and Medawar, P. B. Fibrin suture of peripheral nerves. *Lancet*, 1940, *2:* 126–128.

PENICILLIN IN WARFARE. Special issue *The British Journal of Surgery*, October 1944, *32:* 109–124, 128 figs. (6 in color).

The British Journal of Surgery has just issued the most authoritative statement yet published on the uses of penicillin in war injuries. It includes eighteen separate papers together with a comprehensive bibliography of penicillin, including all reports that have come to their notice up to September 1944. Authors include Major General L. T. Poole, Director of Pathology of the British War Office, Sir Howard Florey and his collaborator, Dr. Norman G. Heatley, Brigadier Hugh Cairns, Lt. Col. Jeffrey, Colonel Elliott Cutler, Major C. R. Wise and Lt. Col. D. M. Pillsbury, and others. Detailed consideration is given to the mode of application of penicillin in war wounds, and throughout this timely record of their war-time experience with the new chemotherapeutic agent emphasis is placed upon early closure of flesh wounds of all types, whether clean or infected.

Lt. Col. James J. Mason Brown makes the impressive statement that of 68 wounds sutured without penicillin 23 per cent went bad, while with 110 comparable wounds sutured after one insufflation of penicillin powder there were no failures. Of 108 obviously infected wounds only 17 per cent failed to close after one penicillin insufflation. He concludes: "The results are so good and the period of morbidity so lessened that all soft-tissue wounds, however small, should be sutured with the aid of penicillin. Recovery is not only rapid, but the nursing care required and the number of dressings have been greatly lessened, leaving the nursing staff much more time to devote to the more serious cases." There is no doubt in the light of this experience that penicillin has utterly transformed our whole concept of the management of war wounds, and it will no doubt similarly transform peace-time traumatic surgery. Who two years ago would have dreamed of closing an extensive and obviously infected flesh wound and expect primary union?

Brigadier Cairns brings us up to date concerning his wide experience in the use of penicillin in head and spinal wounds. He concludes:

"Although the methods of using it are as yet far from standardized, penicillin has proved a most useful substance in the prevention and treatment of infection associated with gunshot wounds of the head; but, however it is applied, it will not be effective unless the dirt, hairs, bone chips, pulped brain, blood-clot, etc., and such missiles as are easily accessible are first removed by surgical excision.

"In recent brain wounds (up to 72 hours old) calcium penicillin can be applied as a powder (5000 units of penicillin per gramme of one of the sulphonamides) followed by primary closure. In 129 cases so treated fatal infection developed in only 2 cases.

"In older brain wounds where pus is already present, penicillin can be applied as follows:— a. After excision and primary closure of the wound sodium or calcium penicillin solution (250 to 1000 units per c.c.) can be instilled through tubes twice daily for 3–5 days. Of 23 old brain wounds so treated only 3 subsequently showed major intracranial infection. b. The wound can be cleaned surgically and left open for 2–3 days with once- or twice-daily application of penicillin powder; secondary suture can then be performed. c. If at operation the scalp is found to be grossly infected the whole wound is surgically excised in the usual way, the scalp is partially closed, and a 2–3 day course of systemic penicillin is given."

Cairns also states that closure of non-penetrating gunshot wounds of the head after excision and insufflation of penicillin is followed by primary healing in 95 per cent of the cases. He emphasizes, however, that careful hemostasis is essential prior to closure lest the penicillin powder be washed away by the oozing blood. Penicillin has also been used to prevent meningitis which might result from the closure of open wounds of the spinal cord.

It is hoped that this important issue of *The British Journal of Surgery* will find its way promptly into the hands of every medical officer charged with the responsibility of handling war-time injuries.

ARCHIVOS DE NEUROCIRUGIA. January to March 1944, *1:* no. 1, 128 pp.

The *Archivos de Neurocirugía* is not a new journal, but a transformation of the *Archivos Argentinos de Neurología*, founded in 1928 by the late Manuel Balado as official organ of the Cátedra de Neurocirugía and the Sociedad de Neurología y Psiquiatría de Buenos Aires.

Director of the newly named journal is Professor Ramón Carrillo of Buenos Aires, Chief of the Cátedra de Neurocirugía, Hospital Nacional de Clínicas (Sala XII). Professor Carrillo for many years, as secretary of the organization, was closely associated with Professor Balado and as his disciple carries on the spirit of the original publication. Collaborators are Dr. A. Asenjo, Santiago, Dr. R. Babbini, Rosario, Drs. P. del Rio Hortega, E. Dowling, J. H. Hanon, R. Orlando and B. Spota, Buenos Aires, Dr. C. Gama, Sao Paulo, Drs. A. Monteiro and J. Ribe Portugal, Rio de Janeiro, Drs. S. Obrador and C. Zuckermann, Mexico, Dr. E. Paglioli, P. Alegre, and Dr. A. H. Schroeder, Montevideo.

Neurosurgery as a specialty was founded in Argentina in 1925 largely through the inspiration of Manuel Balado and Ernesto Dowling. The many friends they made while in the United States remember with pleasure their visits at various clinics, particularly the Mayo Clinic and the clinic of Dr. Harvey Cushing.

Professor Carrillo in his introductory "Nueva epoca" comments on the development of neurosurgery in Argentina in the last twenty years, and points out that sufficient scientific material is produced to express this progress. Though there are journals devoted to neurology and psychiatry, a journal of neurosurgery is needed.

In this first issue the leading article, "La neurocirugía en la Argentina" is by Professor Carrillo. There are four other major contributions and ten reports relating to brain tumors and other disorders of the central nervous system presented at the meetings of the Cátedra de Neurocirugía.

The *Journal of Neurosurgery* extends congratulations to Professor Carrillo and his associates.

CONGRESS OF NEUROSURGERY

Word has been received from South America announcing the first Congress of Neurosurgery, which will take place in Montevideo, Uruguay, from March 1 to 4, 1945. The President of the Acting Committee is Professor Alejandro H. Schroeder, Director of the Instituto de Neurología, Montevideo.

DIRECTORY OF MEDICAL SPECIALISTS

The biographical data of the first two editions of the *Directory of Medical Specialists* included only positions (internships, residencies or assistantships) held during the course of training of men up to the time of their certification by the American Boards, and hospital and medical school staff positions then currently held.

It is desired to extend this data in the Third Edition to include all formal hospital and medical school appointments, with dates held, even though now resigned, as well as records of all military service including commissions and dates, either in World War I, peace-time in the Reserve forces, or in the present war.

Membership or fellowship in national or sectional (not local) special societies, and national general societies with offices held, and dates, in any of these, should be reported.

Membership in recognized international medical societies may be included, but honorary or other membership in foreign medical societies should not be reported.

Reference to the Second Edition (1942) of the Directory may be made for lists of medical societies to be included in one's biographical sketch.

Families or secretaries of men absent in military service are asked to complete or correct previous listings on new forms now being mailed to those eligible for inclusion in the Directory. Only those certified by an official American Board can be included, and there is no charge for this listing.

Communications should be addressed to the Directory of Medical Specialists, 919 North Michigan Avenue, Chicago 11, Illinois.

INDEX TO VOLUME I

Acoustic tumors, symptomatology of, with special reference to atypical features, 371
Akelaitis, A. J. A study of gnosis, praxis and language following section of the corpus callosum and anterior commissure, 94
Alexander, E., Jr. See Campbell, J. B., 365
Angina pectoris, X-ray control of paravertebral injection in, 40
Apparatus: See also Instruments
  Neurosurgical head rest for use in Army and Navy hospitals, 163

Bailey, O. T. See Ingraham, F. D., 23, 171, 252
Ball burr, perforator and, 58
Basilar impression secondary to advanced Paget's disease, 299
Blood plasma, human, products prepared from, 23
Brain, direct observation of, with lucite calvarium, 67
Brain, injuries: See also Cranium; Head
  experimental traumatic cerebral cysts in the rabbit, 182
  histologic studies, late changes: atrophic sclerosis of white matter, 306
  mechanics of trauma with special reference to herniation of cerebral tissue, 190
  microcephalus secondary to birth trauma, 265
  physiological basis of concussion, 103
  traumatic pneumocephalus with spontaneous ventriculograms, 166
Brain, surgery
  gnosis, praxis and language following section of corpus callosum and anterior commissure, 94
  intelligence following prefrontal lobotomy in obsessive tension states, 291
  paralysis in flexion and tremor in the monkey following cortical ablations, 258
  treatment of painful phantom limb by removal of post-central cortex, 156
Brain tumors: See Intracranial tumors
Brenner, C., Friedman, A. P., Merritt, H. H., and Denny-Brown, D. E. Post-traumatic headache, 379

Cairns, H., 201
Campbell, J. B., and Alexander, E., Jr. Eosinophilic granuloma of the skull. Report of a case, 365
Case, T. J. See Walker, A. E., 103
Cathode ray oscilloscope, mechanism of head injuries as studied by, 393
Cerebellum
  extradural cerebellar hematoma, 321
  medulloblastoma with verification nineteen years after onset of symptoms, 252
  tumor in floor of fourth ventricle, bilateral nerve deafness, persistent cough and paroxysmal hyperpnea due to, 325
Cerebrospinal rhinorrhea, surgical repair, 60
Cerebrum: See Brain
Chemotherapy
  in warfare, 201, 451
  of intracranial infections, 76
Coleman, C. C. Peripheral nerve surgery—diagnostic considerations, 123
Concussion, physiological basis of, 103
Corpus callosum and anterior commissure, gnosis, praxis and language following section of, 94
Cough, persistent, due to tumor in floor of fourth ventricle, 325
Craig, W. M. A neurosurgical head rest for use in Army and Navy hospitals, 163
  Peripheral nerve surgery—postoperative rehabilitation, 149
  See Shelden, C. H., 67
Cranium: See also Brain; Head
  basilar impression (platybasia) secondary to advanced Paget's disease, 299
  eosinophilic granuloma of skull, 365
  lucite calvarium, a method of direct observation of the brain, 67
  repair of cranial defects with tantalum, 227
Cushing General Hospital, dedication of, 83
Cushing, Harvey, contributions of, to neurological surgery, 3
Cysts, cerebral, experimental traumatic, in the rabbit, 182

Dahlgren, H. C. Swivel connection for brain suction tip to relieve torsion strain of rubber tubing, 237
Davidoff, L. M. See Mufson, J. A., 45
Deafness, bilateral nerve, due to tumor in floor of fourth ventricle, 325
Delarue, N. C., Linell, E. A., and McKenzie, K. G. An experimental study on the use of tantalum in the sub-dural space, 239
Denny-Brown, D. E. See Brenner, C., 379
Dunbar, H. P., Saltonstall, L., Miles, S., Gillette, G. W., Rankin, F. W., Noyes, E. A., and Fulton, J. F. Dedication of the Cushing General Hospital, Framingham, Massachusetts, 24 January 1944, 83
Dural cyst, intracranial, 211
Dural defects, repair of, with fibrin films, 23

Eosinophilic granuloma of skull, 365
Evans, J. P., and Scheinker, I. M. Histologic studies of the brain following head trauma. IV. Late changes: atrophic sclerosis of the white matter, 306

FALCONER, M. A., and RUSSELL, D. S. Experimental traumatic cerebral cysts in the rabbit, 182
Fibrin foams and films in neurosurgery, 23, 171
FINCHER, E. F. Microcephalus secondary to birth trauma, 265
Florey, H. W., 201
FOSTER, M. E., JR. See Haymaker, W., 211
FREEMAN, W. See Watts, J. W., 291
FRIEDMAN, A. P. See Brenner, C., 379
FULTON, J. F. See Dunbar, H. P., 83

GENTRY, R. W. See White, J. C., 40
GERMAN, W. J. Cerebrospinal rhinorrhea—surgical repair, 60
GILLETTE, G. W. See Dunbar, H. P., 83
Gnosis, praxis and language following section of corpus callosum and anterior commissure, 94
GRANT, F. C. Operative results in intervertebral discs, 332
GURDJIAN, E. S., and LISSNER, H. R. Mechanism of head injury as studied by the cathode ray oscilloscope. Preliminary report, 393
DE GUTIÉRREZ-MAHONEY, C. G. The treatment of painful phantom limb by removal of postcentral cortex, 156

HAMBY, W. B. A tantalum cranial clip, 331
See Shinners, B. M., 117
Harvey Cushing Society, transactions of, 338
HAYMAKER, W., and FOSTER, M. E., JR. Intracranial dural cyst with report of a case, 211
Headache, post-traumatic, 379
Head, injuries: See also Brain; Cranium
cerebrospinal rhinorrhea, surgical repair, 60
dark adaptation, negative after images, tachistoscopic examinations and reaction time in, 243
mechanism of, as studied by cathode ray oscilloscope, 393
post-traumatic headache, 379
Hematoma, extradural cerebellar, 321
Hemostatic agents
fibrin foams, 23
muscle, comparison of, with fibrin foam, 171
Hemostats, galea, method of holding, in craniotomies, 392
HOLBOURN, A. H. S. The mechanics of trauma with special reference to herniation of cerebral tissue, 190
HORRAX, G. Some of Harvey Cushing's contributions to neurological surgery, 3
See Olsen, A., 371
Hyperpnea, paroxysmal, due to tumor in floor of fourth ventricle, 325

INGRAHAM, F. D., and BAILEY, O. T. Cerebellar medulloblastoma with verification nineteen years after the onset of symptoms, 252
The use of products prepared from human fibrinogen and human thrombin in neurosurgery. Fibrin foams as hemostatic agents; fibrin films in repair of dural defects and in prevention of meningocerebral adhesions, 23
——, BAILEY, O. T., and NULSEN, F. E. Studies on fibrin foam as a hemostatic agent in neurosurgery, with special reference to its comparison with muscle, 171
Injection, paravertebral, X-ray control of, in angina pectoris, 40
Instruments: See also Apparatus
method of holding galea hemostats in craniotomies, 392
perforator and ball burr, 58
swivel connection for brain suction tip, 237
tantalum cranial clip, 331
Intelligence following prefrontal lobotomy in obsessive tension states, 291
Intervertebral discs
differential diagnosis of intraspinal tumors and protruded intervertebral discs and their surgical treatment, 275
operative results in, 332
protruded lumbar, results of surgical removal of, 117
Intracranial infections, chemotherapy of, 76, 201, 451
Intracranial tumors
acoustic, symptomatology of, with special reference to atypical features, 371
dural cyst, 211
extradural cerebellar hematoma, 321
medulloblastoma, cerebellar, with verification nineteen years after onset of symptoms, 252
meningiomas, multiple, 45
tumor in floor of fourth ventricle, bilateral nerve deafness, persistent cough and paroxysmal hyperpnea due to, 325

KANTROWITZ, F. A. A method of holding galea hemostats in craniotomies, 392
KAPLAN, A. Traumatic pneumocephalus with spontaneous ventriculograms. Report of a case, 166
KENNARD, M. A. See Welch, W. K., 258
KOLLROS, J. J. See Walker, A. E., 103

Language
gnosis, praxis and language following section of corpus callosum and anterior commissure, 94
LINELL, E. A. See Delarue, N. C., 239
LISSNER, H. R. See Gurdjian, E. S., 393
LOVE, J. G. The differential diagnosis of intraspinal tumors and protruded intervertebral disks and their surgical treatment, 275
Lucite calvarium, processing techniques, 67

MCKENZIE, K. G. A perforator and ball burr, 58
See Delarue, N. C., 239

MEACHAM, W. F. See Pilcher, C., 76
Medulloblastoma, cerebellar, with verification nineteen years after onset of symptoms, 252
Meninges
intracranial dural cyst, 211
repair of dural defects with fibrin films, 23
Meningiomas, multiple, 45
Meningitis, pneumococcal, treatment of, by penicillin, 76
Meningocerebral adhesions, prevention of, with fibrin films, 23
MERRITT, H. H. See Brenner, C., 379
Microcephalus secondary to birth trauma, 265
MILES, S. See Dunbar, H. P., 83
MUFSON, J. A., and DAVIDOFF, L. M. Multiple meningiomas. Report of two cases, 45
Muscle, comparison of fibrin foam as hemostatic agent, 171

Nerves, peripheral, regeneration, technology of: sutureless tubulation and related methods of nerve repair, 400
Nerves, peripheral, surgery
diagnostic considerations, 123
postoperative rehabilitation, 149
sutureless reunion of severed nerves with elastic cuffs of tantalum, 219
technical considerations, 133
Neurological surgery: See also Apparatus; Instruments
fibrin foams and films in, 23, 171
Harvey Cushing's contributions to, 3
NOYES, E. A. See Dunbar, H. P., 83
NULSEN, F. E. See Ingraham, F. D., 171

OLSEN, A., and HORRAX, G. The symptomatology of acoustic tumors with special reference to atypical features, 371

Paget's disease, advanced, basilar impression (platybasia) secondary to, 299
Paralysis in flexion and tremor in the monkey following cortical ablations, 258
Paravertebral injection, X-ray control of, in angina pectoris, 40
Penicillin, treatment of pneumococcal meningitis by, 76
Penicillin in warfare, reviews
British Journal of Surgery, 451
Florey and Cairns report, 201
Perforator and ball burr, 58
Phantom limb, painful, treatment of, by removal of post-central cortex, 156
PILCHER, C., and MEACHAM, W. F. The chemotherapy of intracranial infections. IV. The treatment of pneumococcal meningitis by intrathecal administration of penicillin, 76
Platybasia secondary to advanced Paget's disease, 299
Pneumocephalus, traumatic, with spontaneous ventriculograms, 166
Praxis
gnosis, praxis and language following section of corpus callosum and anterior commissure, 94
PUDENZ, R. H. See Shelden, C. H., 67

RANKIN, F. W. See Dunbar, H. P., 83
RESTARSKI, J. S. See Shelden, C. H., 67
Reviews
Archivos de Neurocirugía, 452
Penicillin in warfare, British Journal of Surgery, 451
Investigation of war wounds. Penicillin. Florey, H. W., and Cairns, H., 201
Rhinorrhea, cerebrospinal, surgical repair, 60
ROBERTSON, R. C. L. Repair of cranial defects with tantalum, 227
Roentgen rays
control of paravertebral injection in angina pectoris, 40
traumatic pneumocephalus with spontaneous ventriculograms, 166
RUESCH, J. Dark adaptation, negative after images, tachistoscopic examinations and reaction time in head injuries, 243
RUSSELL, D. S. See Falconer, M. A., 182

SALTONSTALL, L. See Dunbar, H. P., 83
SCHEINKER, I. M. See Evans, J. P., 306
Sclerosis
atrophic sclerosis of white matter following head trauma, histologic studies of, 306
SHELDEN, C. H., PUDENZ, R. H., RESTARSKI, J. S., and CRAIG, W. M. The lucite calvarium—a method for direct observation of the brain. I. The surgical and lucite processing techniques, 67
SHINNERS, B. M., and HAMBY, W. B. The results of surgical removal of protruded lumbar intervertebral discs, 117
Skull: See Cranium
Society transactions, Harvey Cushing Society, 338
Spinal cord tumors, differential diagnosis of intraspinal tumors and protruded intervertebral disks and their surgical treatment, 275
Spine: See Intervertebral discs
SPURLING, R. G. Peripheral nerve surgery—technical considerations, 133
Subdural space, experimental study on use of tantalum in, 239
Swivel connection for brain suction tip, 237

Tantalum
cranial clip, 331
elastic cuffs, sutureless reunion of severed nerves with, 219
experimental study on the use of, in subdural space, 239

repair of cranial defects with, 227
Transactions of The Harvey Cushing Society. Thirteenth annual meeting held at The Commodore, New York City, May 17 and 18, 1944, 338
Trauma: See Brain; Cranium
Tremor
paralysis in flexion and tremor in the monkey following cortical ablations, 258
Tumors: See Intracranial tumors
TURNBULL, F. Extradural cerebellar hematoma. A case report, 321

Ventriculograms, spontaneous, in traumatic pneumocephalus, 166
Vision
dark adaptation, negative after images, tachistoscopic examinations and reaction time in head injuries, 243

WALKER, A. E., KOLLROS, J. J., and CASE, T. J. The physiological basis of concussion, 103
WATTS, J. W., and FREEMAN, W. Intelligence following prefrontal lobotomy in obsessive tension states, 291
WEISS, P. Sutureless reunion of severed nerves with elastic cuffs of tantalum, 219
The technology of nerve regeneration: a review. Sutureless tubulation and related methods of nerve repair, 400
WELCH, W. K., and KENNARD, M. A. Paralysis in flexion and tremor in the monkey following cortical ablations, 258
WELLER, D. Bilateral nerve deafness, persistent cough and paroxysmal hyperpnea due to a tumor in the floor of the fourth ventricle, 325
WHITE, J. C., and GENTRY, R. W. Radiographic control for paravertebral injection of alcohol in angina pectoris, 40
WYCIS, H. T. Basilar impression (platybasia). A case secondary to advanced Paget's disease with severe neurological manifestations. Successful surgical result, 299

X-rays: See Roentgen rays

LIBRARY
WEST VIRGINIA UNIVERSITY